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ON THE DEVELOPMENT OF THE ACCOMMODATIVE POWER OF THE HUMAN LENS.*

By E. TREACHER COLLINS.

THE accommodative power of the human lens was demonstrated by Helmholtz to be due to its elastic fibres being maintained in a state of tension, the relaxation of which brought about an increased convexity of its anterior surface. The way in which this state of tension of the lens fibres is developed forms the subject of this paper.

The relaxation of the tension of the lens fibres in accommodation was stated by Helmholtz to be effected by slackening of the suspensory ligament of the lens, and this theory, though contested by some, is supported by much clinical and experimental evidence. The development of the accommodative power of the lens must be looked for, therefore, in the development of its suspensory ligament.

In a paper on that subject published in vol. xiii, pt. 1 of these reports, I gave a table showing the diameter of a series of eyeballs and their lenses from the 4th to the 9th month of fœtal life.

At the 4th month the ciliary body is in contact with the

* This paper was read at the Tenth International Congress of Ophthalmology held at Lucerne. It is republished here, together with illustrations not previously reproduced. These illustrations are from photo-micrographs kindly taken for me by Mr. E. Collier Green, of Derby.

sides of the lens. At the 9th month the transverse diameters of the eyeball and the lens are double what they are at the 4th month, and in the adult they are treble what they are at the 4th month. As the eyeball and lens increase in size in this proportion, and as the eyeball is larger to begin with, it follows that as the eye develops there must be a gradual separation of the ciliary body away from the sides of the lens.

It is natural to suppose that the adhesions which join the lens to the ciliary body, viz., the fibres of the suspensory ligament, would be first formed while those structures are in contact, and that they would be stretched out and rendered tense as they become separated.

Sections of a human fœtal eye in which, what ultimately develops into the *pars ciliaris retinæ* is in contact with the lens, show, intervening and lying in contact with both, some tissue composed of spindle shaped cells of mesoblastic origin (Pl. II, Fig. 1).

In this tissue is subsequently developed the network of blood vessels which forms a vascular sheath to the lens.

In sections of fœtal eyes of a later date where the rudimentary ciliary body has become separated from the sides of the lens, in the situation of the suspensory ligament elongated cells may sometimes be seen, or fibres of the suspensory ligament with nuclei attached to them (Pl. IV, Fig. 1).

Similar elongated cells or fibres with nuclei on them are met with in congenital microphthalmic eyes in the situation of the suspensory ligament, evidently due to its arrested development. These malformations are referred to again more in detail at the end of this paper.

There seems then considerable evidence to show that the suspensory ligament of the lens is originally derived from cells which become lengthened out into fibres and lose their nuclei.

There are two possible sources of these cells:—

1. The mesoblastic cells already referred to as surrounding the lens capsule at a very early period of fœtal life.
2. The neural epiblastic cells composing the *pars ciliaris retinæ*.

A priori, seeing that the suspensory ligament is of the nature of a connective tissue it would be natural to suppose that it was derived from mesoblast. Its intimate association with the vitreous humour is also in favour of the two structures having the same genetic origin.

Schoen* and Terrien,† however, as the result of their histological researches, regard the fibres of the suspensory ligament as derived from the epithelial cells forming the *pars ciliaris retinæ, i.e.,* making them analogous to the fibres of Müller which form the supporting connective tissue of the retina.

I have myself been unable to arrive at any certain conclusion in favour of one or other of these views, and fortunately it is immaterial for the purpose of this paper which is ultimately found to be correct.

The most recent investigations‡ into the arrangement of the suspensory ligament in the human eye have shown that the bundles of fibres of which it is composed do not pass straight out from the sides of the lens to the ciliary body, but that they cross one another. Thus fibres which are most anterior in their attachment to the lens capsule pass to the hindermost part of the ciliary body, whilst those coming from the foremost part of the ciliary body pass to the posterior part of the lens capsule.

It has been possible to differentiate several groups of fibres and describe them by distinctive names. Thus, the fibres which pass from the non-plicated part of the ciliary body to the anterior part of the lens capsule, and which lie in the valleys between the ciliary processes, are called *the orbiculo-antero-capsular fibres.* Those which pass from the *ora serrata* and the hindermost part of the non-plicated part of the ciliary body to the posterior part of the lens capsule are *the orbiculo-postero-capsular fibres.* Those passing from the apices of the ciliary processes to the posterior part of the

* Anatom. Anzeiger, Bd. x, 1895.

† Archives d'Ophtal., T. xviii, 1898, p. 555.

‡ Garnier, Archiv f. Augenheilk., Bd. xxiv, 1892.

lens capsule, between the bundles of the orbiculo-antero-capsular fibres, are *the cilio-postero-capsular fibres;* and those running directly inwards from the ciliary processes to the lens capsules are called *the cilio equatorial fibres.* (Pl. I, Figs. 1 and 2).

Some writers have also described certain *accessory fibres* passing from the non-plicated part of the ciliary body to the ciliary processes, from one ciliary process to another, or from the ciliary body to adjacent fibres. It is very possible, however, that these so-called accessory fibres are really only some of the other bundles of fibres cut obliquely.

In order to understand how this interlacement of the different bundles of fibres of the suspensory ligament is brought about, it is necessary to examine the relation which the different parts of the ciliary body bear to the sides of the lens at different periods in fœtal life. When the lens vesicle is first formed and has become cut off from the surface epiblast there is no ciliary body and no iris. The anterior extremity of the optic vesicle at that time corresponds to what afterwards becomes the *ora serrata,* and it lies in contact with the antero-lateral portion of the newly formed lens vesicle. (Pl. II, Fig. 1).

As the iris and ciliary body bud out of the anterior extremity of the secondary optic vesicle and the anterior extremity of the rudimentary choroid, that part of the retina which corresponds ultimately to the *ora serrata* gets displaced backwards along the side of the lens, until, from being in contact with the anterio-lateral part of that structure it comes to lie in contact with the posterio-lateral part. (Pl. II, Fig. 2).

At first the ciliary body has no ciliary processes, at that time being represented only by a short straight unfolded area lying in close apposition with the sides of the lens.

Folds commence to bud out from the ciliary body at its anterior extremity, *i.e.*, where it joins the rudimentary iris. These folds extend inwards and backwards, passing between the side of the lens and the unfolded area of the ciliary body,

which by that time have become somewhat separated. The apex of these folds extends so far back along the side of the lens as to reach its posterior lateral parts. (Pl. III, Fig. 1.)

In the later growth of the eye both plicated and non-plicated parts of the ciliary body become separated away from the sides of the lens. The development of the anterior chamber, and consequent displacement backward of the lens, tends still further to draw the ciliary processes away from a level with its posterior surface to a level with its anterior surface. (Pl. III, Fig. 2.)

The final stage in the development of the ciliary body, and one which is not complete until some time after birth, consists in the lengthening out of the non-plicated part of the ciliary body, and the further displacement backwards of it and of the *ora serrata* away from the lens. (Pl. IV, Figs. 1 and 2.)

It will thus be seen that different portions of the ciliary body are in contact with the sides of the lens at different times, and that adhesions which form between them must originate at different times.

The first to be formed are those passing between the anterior part of the lens capsule and the non-plicated part of the ciliary body, which as these structures grow apart become stretched out into the orbiculo-antero-capsular fibres of the suspensory ligament.

Next in formation are the adhesions between the posterior part of the non-plicated part of the ciliary body, together with the *ora serrata*, and the posterior part of the lens capsule which later result in the orbiculo-posterio-capsular fibres.

As the ciliary processes commence to form and grow, extending backwards between the rudimentary non-plicated part and side of the lens, they pass between the several bundles of the orbiculo-antero-capsular fibres, which latter come ultimately to lie in the valleys between the ciliary processes.

While the ciliary processes lie in contact with the sides

and posterior lateral portion of lens, adhesions form, which on separation of those structures become lengthened out into cilio-posterio-capsular fibres and cilio-equatorial fibres.

The growth of the ciliary body away from the side of the lens, not only tends to stretch out and lengthen adhesions which have formed between them, but also causes considerable traction on the capsule of the lens.

We find that in early fœtal life, when the ciliary body is in contact with the lens the latter is round. As the ciliary body grows away from it, its lateral diameter increases considerably out of proportion to its antero-posterior diameter.

If this lateral traction on the lens is exerted to an abnormal extent, as it is in the expansion of the ciliary region in buphthalmic eyes, then the disproportion between its lateral and antero-posterior diameters becomes markedly increased.

The growth of the ciliary processes away from the posterior lateral portion of the lens, and the displacement of the lens backwards on the formation of the anterior chamber causes, through the cilio-posterior capsular fibres, considerable traction on the posterior capsule (Fig. *a* in text).

The growth backwards away from the sides of the lens of the non-plicated portion of the ciliary body causes, through the orbiculo-antero-capsular fibres, considerable traction on the anterior capsule.

There are thus developed in the growth and expansion of the eye forces dragging on the posterior part of the lens capsule forwards and outwards, and on the anterior part of the lens capsule backwards and outwards.

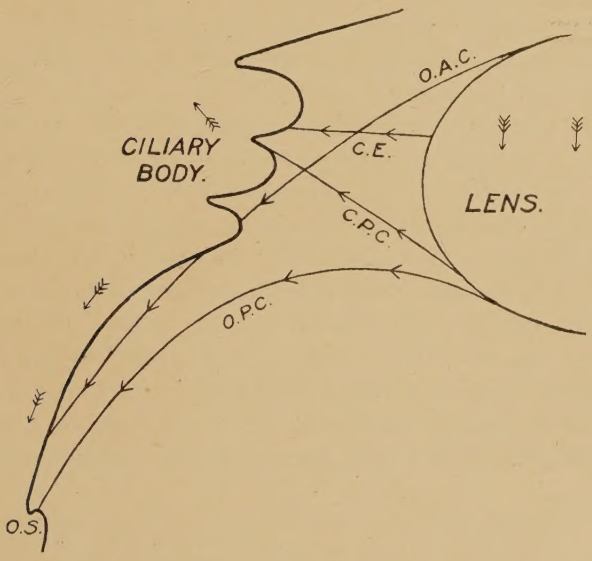
The effect of this on the elastic curved lens fibres is to cause them to become more bent and kept in a state of tension. A state of tension which is only relaxed when by the contraction of the ciliary muscle the suspensory ligament is slackened and the pull on the capsule relieved.

It is interesting to note, in connection with the development of the ciliary body in the human eye, that the different temporary stages through which it passes are

formed as permanent conditions in lower animals. In the lowest fish, eels, and also in some species of carp, there is no ciliary body, the retina ends at the base of the iris. (Pl. V, Fig. 1).

In the following teleostean fish, whiting (*gadus merlangus*), cod (*gadus morrhua*), mackerel (*scomber scombrus*), and plaice (*pleuronictis platessa*), the termination of the retina does not extend quite so far forwards, it does not quite reach up

FIG. *a*.



to the root of the iris. In eels and the carp it extends as far as, or further than, the anterior margin of the cartilage in the sclerotic, in the others it is situated behind that point.

In the following elasmobranch fish, the thornback (*raja clavata*), the lesser spotted dog fish (*scyllium catulus*), and the spring dog fish (*acanthus vulgaris*), the displacement backwards of the anterior termination of the retina is still more marked. The area which extends between it and the root of the iris is thrown into shallow folds laterally, and has

some slight elevations and depressions antero-posteriorly. It is lined by a single row of unpigmented cells, the *pars ciliaris retinæ*.

In the eyes of the following reptiles, the land tortoise (*testudo Græca*), the slow worm (*anguis fragilis*) and the sand lizard (*lacerta agilis*), the ciliary body is represented by a short area lined by a single row of unpigmented cells, situated between the root of the iris and termination of the retina without any elevations or depressions in it. (Pl. V, Fig. 2). In the common ringed snake (*coluber natrix*) there is a well marked simple fold protruding inwards and backwards in the ciliary region, lined by columnar shaped unpigmented cells. (Pl. VI, Fig. 1.)

All mammals, including the ornithorrynchus and echidna, have well marked ciliary processes showing in antero-posterior sections well developed folds. The amount of plication of the ciliary processes varies considerably in different species, but in all except the quadrumana the extent of the non-plicated area is markedly less than in man.

The following table shows that the distance between the root of the iris and the *ora serrata* compared to the antero-posterior diameter of the globe is greater in the quadrumana and man than in other mammals. That is to say, that in those mammals who have greatest amount of accommodative

	Antero posterior diameter of eyeball. mm.	Distance between root of iris and ora serrata. mm.
Man	24·8	6
Chimpanzee	19	4·25
Rhesus monkey (India)	19·5	5
Capuchin monkey (South America)	18·5	4·25
Cat	22	3·5
Sheep	28	6
Bullock	35	6·5
Pig	22	4
Rabbit	19	2

power, there is the widest separation of the *ora serrata* from the anterior surface of the lens and consequently the greatest amount of drag on the anterior capsule.

In the examination of sections of human microphthalmic eyes it is frequently found that there has been an arrested development of the ciliary body and suspensory ligament.

Relations of the ciliary body to the sides of the lens which are only temporary phases in fœtal life are found, and evidence of the cellular origin of the fibres of the suspensory ligament is met with.

In one microphthalmic eye of which I have recorded a description, the vascular system of the vitreous and lens, which exists during fœtal life, had failed to become obliterated, a complete network of blood-vessels encircled the lens. The ciliary processes had failed to develop, the *pars ciliaris retinæ* and *ora serrata* were in contact with the sides of the lens. In the expansion of the globe their adhesion to the lens had remained so firm, that the two layers of the secondary optic vesicle became torn apart in the ciliary region, instead of its inner layer growing away from the lens. In other microphthalmic eyes, where the central hyaloid artery has remained patent and where the anterior part of the vitreous has developed atypically, I have found the ciliary processes passing backwards and adherent to the posterior lateral part of the lens.

I have also found that the retina at the *ora serrata* has failed to grow backwards away from the back of the lens, a fold having become formed in it in that position. An abnormally short non-plicated area of the ciliary body is a frequent accompaniment of microphthalmia.

I have sections of microphthalmic eyes in which the apices of the ciliary processes are in close proximity to the lens capsule, and where some elongated cells join the two structures. Also sections of several eyes in which stretching between the ciliary body and the lens capsule are fibres, like those of the suspensory ligament but with nuclei on them. Some of these at their insertion into the ciliary body are seen

to pass definitely into elongated cells (*vide* Figs. 1 and 2, pp. 84 and 85, vol. xiii, of the R.L.O.H. Reports).

In one specimen in which the lens was congenitally displaced, in the interval between the ciliary body and lens on the opposite side to which the latter was drawn, there were no fibres of suspensory ligament, but lying in the circumlental space in front of some atypically developed vitreous were some elongated cells and nucleated fibres. (Pl. VI, Fig. 2.)

Description of Plates I—VI.

Plate I, Figs. 1 and 2.—Show the suspensory ligament of the lens in sections of a normal human eye. The foremost fibres shown in Fig. 2 are the orbiculo-antero-capsular fibres, the prolongation of which backwards to the non-plicated part of the ciliary body is shown in Fig. 1. The hindermost fibres shown in both figures are the orbiculo-postero-capsular fibres. The cilio-equatorial fibres can be seen in Fig. 2 crossing the orbiculo-antero-capsular fibres, and passing direct from the ciliary processes to the equator of the lens. The cilio-postero-capsular fibres are shown in Fig. 2 and at their commencement in Fig. 1. They cross the cilio-equatorial and orbiculo-antero-capsular fibres, and pass to the back of the lens.

Plate II, Fig. 1.—Shows a section through the eye of a human fœtus of the 6th week. The lens vesicle has become shut off from the surface epiblast. There is no iris or ciliary body. The termination of the secondary optic vesicle touches the antero-lateral part of the lens. The ciliary body and iris grow out from it, and what is at this stage its termination ultimately corresponds to the *ora serrata*. Some tissue, composed of spindle-shaped cells which becomes the fibro-vascular sheath of the lens, lies between the sides of the lens capsule and the inner layer of the secondary optic vesicle.

Fig. 2.—Shows a section of fœtal pig's eye. The lens is in contact with the back of the cornea. The iris and ciliary body have commenced to grow out of the anterior part of the secondary optic vesicle. The part which would have ultimately corresponded to the *ora serrata* lies opposite the equator of the lens.

Plate III, Fig. 1.—Shows a section through the anterior part of a human fœtal eye of about the 10th week. The eyelids are seen united over the front of the cornea. The lens is in contact with the back of the cornea. The iris is beginning to grow and insinuate itself between the lens and cornea. The ciliary process is seen beginning to grow out with a direction backwards towards the postero-lateral part of the lens. In the preparation of the specimen the pigmented

layer of the ciliary body has become slightly separated away from the *pars ciliaris retinæ ;* the latter lies in close contact with the side of the lens.

Fig. 2.—Shows a section through a portion of a human fœtal eye of between the 4th and 5th month. The lens is separated away from the cornea, and the ciliary processes from the side of the lens. The most anterior of the ciliary processes points backwards in the direction of the posterior lateral part of the lens. A piece of a cellular adhesion, which stretched between them, is shown attached to the postero-lateral part of the lens. There is no non-plicated part of the ciliary body.

Plate IV, Fig. 1.—Shows a section through a portion of a human fœtal eye of between the 4th and 5th month. The lens is separated from the back of the cornea. The ciliary processes have grown a short way away from the side of the lens ; stretching between them can be seen the fibres of the suspensory ligament with a few nuclei faintly showing on them. There is no non-plicated part of the ciliary body. The retina, in preparing the specimen, has become detached ; the *ora serrata* is situated at the termination of the ciliary processes.

Fig. 2.—Shows a section through the ciliary body and suspensory ligament in a normal adult human eye. The wide separation of the *ora serrata* from the ciliary processes and from the side of the lens is seen. It is due to the lengthening out of the non-plicated part of the ciliary body.

Plate V, Fig. 1.—Shows a section through the angle of the anterior chamber and anterior termination of the retina of the eye of an eel. The posterior layers of the cornea, in the preparation of the specimen, have become spaced out. The anterior chamber is very shallow. There is no ciliary body. The anterior termination of the retina extends up to the root of the iris, almost as far as the angle of the anterior chamber.

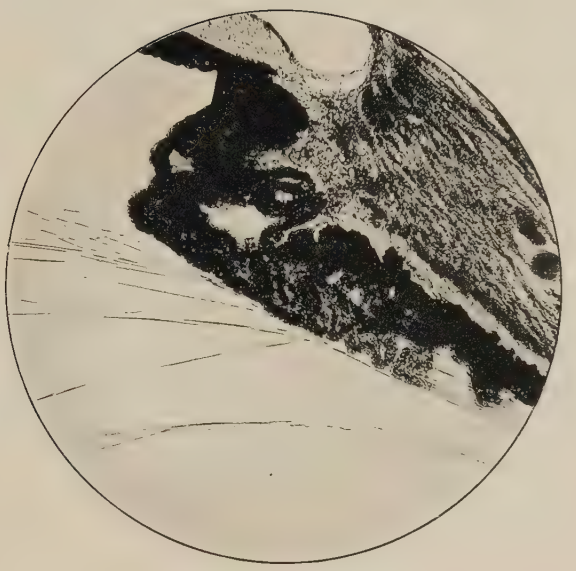
Fig. 2.—Shows a section through the eye of a sand lizard. There is a small non-plicated area seen between the root of the iris and the anterior termination of the retina.

Plate VI, Fig. 1.—Shows a section through the angle of the anterior chamber and ciliary region of the eye of a common ringed snake. The anterior chamber is very shallow. Between the root of the iris and the anterior termination of the retina one simple fold protrudes inwards, constituting the ciliary body.

Fig. 2.—Shows a section through ciliary region of a human eye which had a congenitally displaced lens. Between the ciliary processes and the side of the lens, instead of the fibres of the suspensory ligament, some elongated cells and nucleated fibres are seen.

Description of Fig. *a* in Text.

This diagram is to represent the direction of the different forces which come into play in the development of the suspensory ligament. The letters are the initials of the names of the different sets of fibres in the suspensory ligament, which are here each represented by a single line. The arrows and arrow heads show the direction in which traction is exerted on the lens. The arrows on the lens itself indicate that on the formation of the anterior chamber it is displaced backwards.



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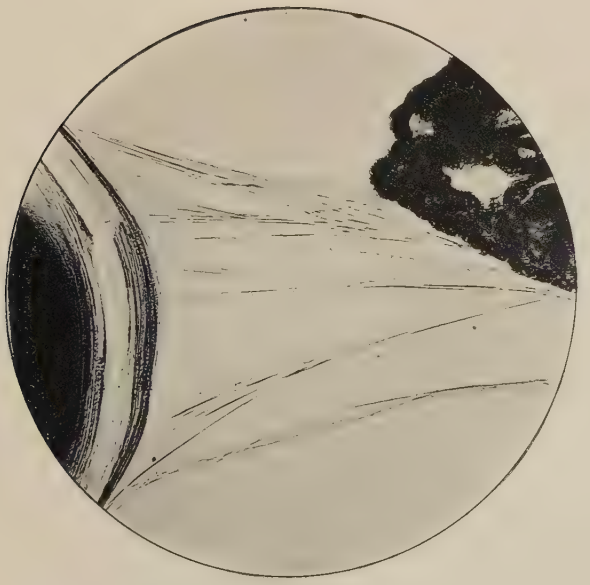

FIG. 2.

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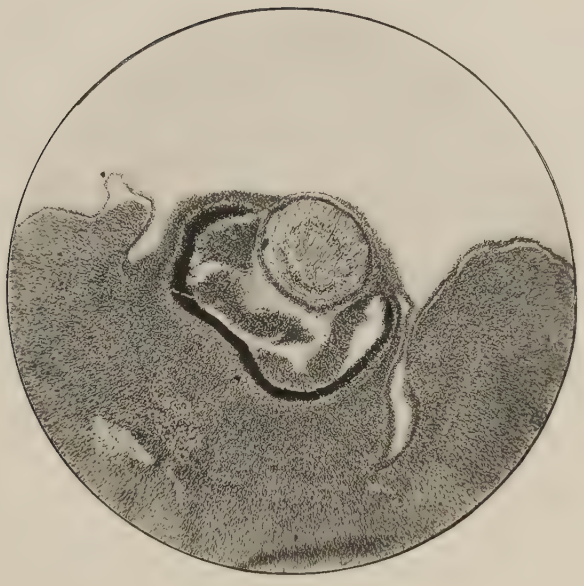

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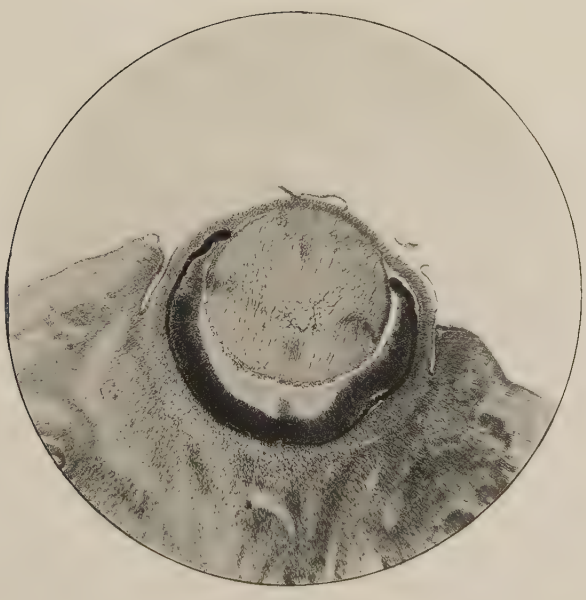

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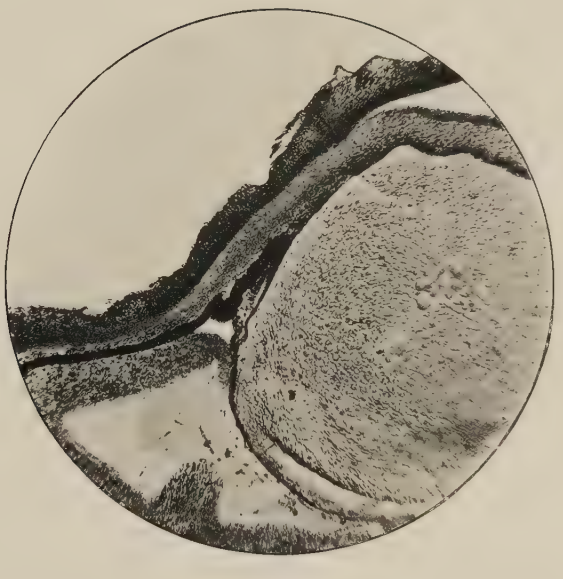

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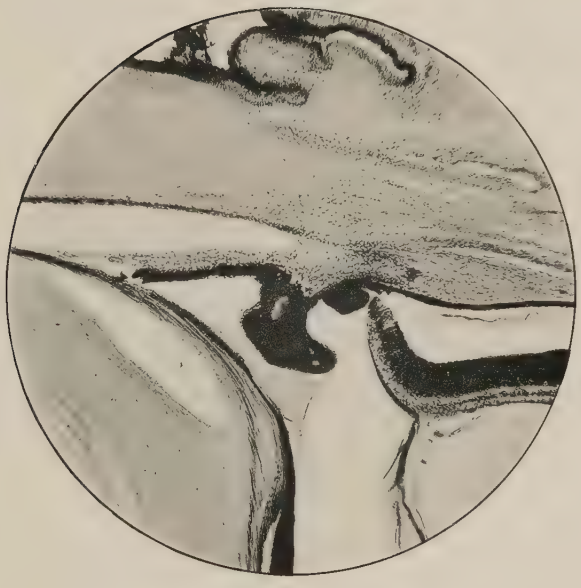

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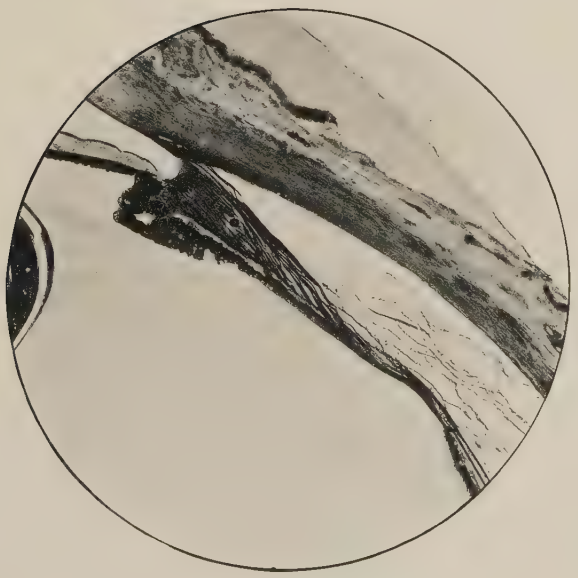

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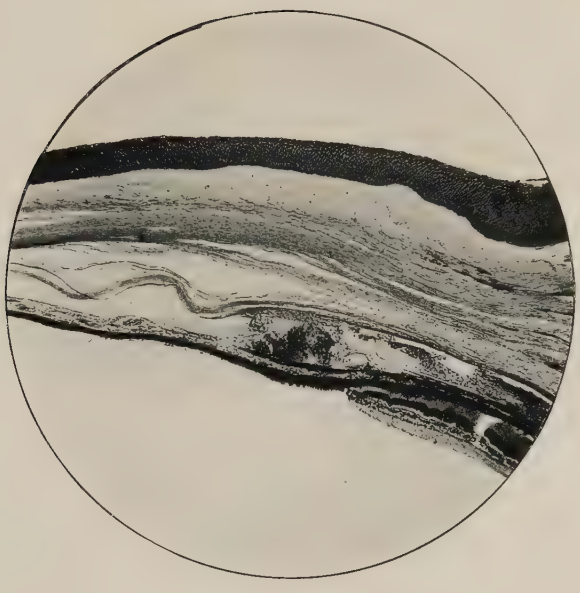

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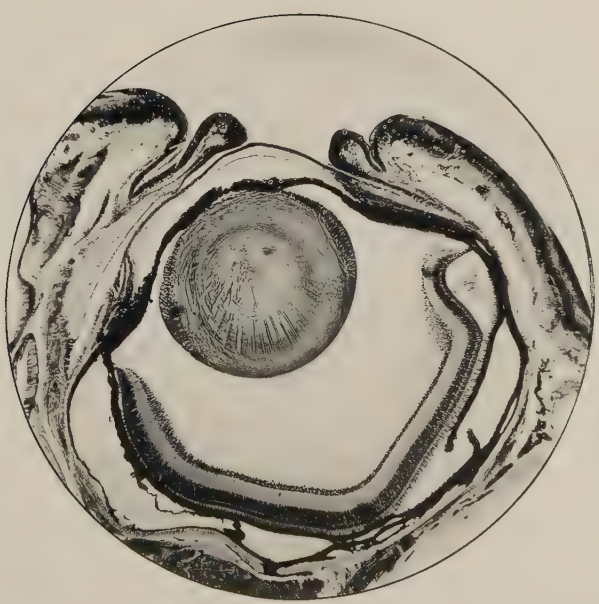

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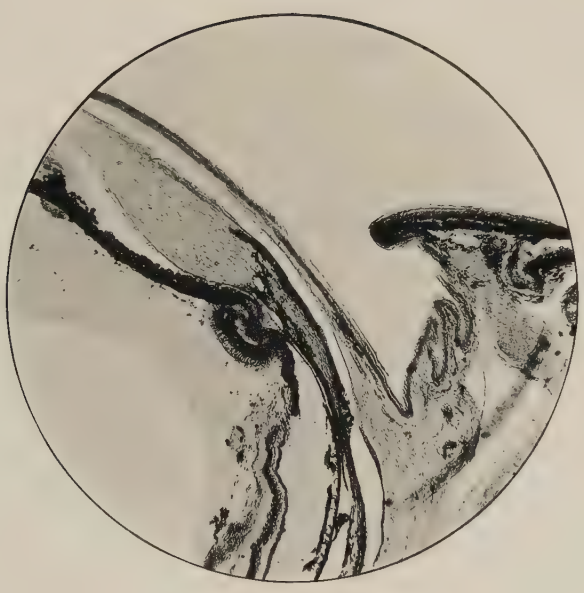

FIG. 1.

FIG. 2.

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TWO CASES OF COLLOID (HYALIN) DEGENERATION OF TARSUS AND CONJUNCTIVA.

By H. Herbert, Major, I.M.S.

With every desire to avoid contributing to the confusion that exists among hyalin and allied degenerations, the term "colloid" is here retained because, apart from the reasons given* in the description of an earlier case of conjunctival degeneration, neither of the two cases now related, nor the one just referred to, can be classed strictly as belonging either to the hyalin or amyloid subdivisions of v. Recklinghausen's colloid group. As is so often the case, the amyloid reactions obtained (in sections of fixed and hardened tissue only) were partial and incomplete.

Case I.—A Hindoo woman of 39 years. Right upper lid alone affected. Lid swollen and drooping from considerable thickening and vertical enlargement of tarsus. The maximum vertical measurement of the latter was apparently† 1·6 cm. towards its outer end. Eversion of the lid was difficult, and caused a little bleeding from a few points on the conjunctival surface. The tarsus and its covering of conjunctiva presented a yellowish, somewhat translucent appearance, except where there was a patch of opaque scar-tissue in the conjunctiva. The same yellowish tint and translucence were also noticeable in the conjunctiva for a little distance above the tarsus. A good deal of the firm wax-like tissue was removed; the knife cut into it very easily, and there was little bleeding. The conjunctiva

* (1) The fact that the same changes in the skin are known by dermatologists as colloid degeneration, and (2) the suitability of the term to define what is mainly a derivative of collagen (white fibrous tissue). See Trans. Ophth. Soc., vol. xxii, 1902.

† It was impossible to define exactly the limits of the tarsus in sections. The vertical extent here given probably therefore includes a little of the neighbouring thickened tissues.

presented no abnormality beyond the patch of scarring above mentioned, and slight papillary roughness and general injection.

CASE II.—Male Hindoo of 25 years. The right upper lid was here also the one affected; its upper part only was noticeably swollen. On eversion of the lid the upper half of the enlarged tarsus was found considerably thickened, and made up mainly of two petrified masses, covered only by conjunctiva. When the conjunctiva was divided these masses shelled out easily, their immediate surroundings being of a loose, spongy nature. The larger of the two measured 1 cm. in length and 3 mm. in thickness; the other mass was much smaller. A few microscopic spicules and strips of true bone were afterwards found in sections of the decalcified larger mass, but none in the smaller one. The neighbouring thickened tarsus had undergone colloid change, as had also the conjunctiva and subconjunctival tissues for some little distance above.

The very considerable extent of smooth swelling above could not be fully seen till after the excision of much of the enlarged tarsus. From the swollen retrotarsal conjunctiva, when incised, much soft wax-like material could be readily expressed; but the tissues were decidedly vascular, and the colloid change not sufficiently advanced to produce the semi-translucent clinical appearance so noticeable in Case I.

There was fairly advanced pannus on this side; none in the other eye. In the conjunctiva some traces of cicatricial tissue and slight thickening and papillary roughness, but no follicles; similar changes, less marked, on the other side.

A full account of the changes found in sections need not be given, but a few special points must be noticed regarding firstly the soft parts, and secondly the petrified and ossified tissues.

A. Soft Parts.

The colloid change is most advanced* in Case I, corresponding with clinical appearances. No elastic tissue can be

* The biuret reaction was readily obtainable in the colloid substance of this case, though not of Case II (the only sections tested in Case II were from the retrotarsal conjunctiva).

found in the parts examined from this Case, even in the blood-vessels, and the only remains of collagen (white connective tissue fibres) in the colloid blocks, as shown by acid fuchsin, are very blurred and indistinct; and in places (see Pl. VII, Fig. 1) there is nothing now recognisable of the conjunctiva but the epithelium, though elsewhere there is still a fairly thick adenoid layer. Tracts of cells, mostly plasma cells and cells transitional between plasma cells and fixed connective tissue cells, penetrate throughout the altered tarsus.

The results of the *tests for amyloid* are as follows:— The greater part of the colloid substance stains reddish-brown with iodine, but a few of the blocks in Case I at once acquire a pale greenish tint (!), which is not altered by treatment with dilute sulphuric acid. The acid changes the reddish-brown colour to dark brown, especially dark in Case I. In some of the much altered blood-vessels of the retrotarsal subconjunctival tissue of Case II small scattered areas (see Pl. VII, Fig. 2) within the still recognisable "internal elastic lamina" become lilac-coloured with thionin. Negative results were obtained in both cases with gentian and methyl violet, methyl green, and iodine green, used both in weak solution for 24 hours, and in strong solution.

Cellular degeneration.—Divergent views as to the part played by the cells in colloid degeneration arise from three sources: (1) the absence of distinctive staining reactions for the colloid material; (2) close contact of some degenerating connective tissue cells (and endothelial cells?) with colloid blocks; and (3) the uncertainty as to whether homogeneous material lying in cells has been merely taken up by the cells or formed in the cells.

In the adenoid layer of the retrotarsal conjunctiva of Case II where the changes are not very advanced, the breaking up of plasma cells is much in evidence. But the vacuoles seen in the cells are quite clear and unstained. Lying free among the cells there are numerous small rounded particles. Many of them display their cellular origin by colouring deeply with polychrome methylene blue; other particles

show a preference for orceïn in varying degree, and possibly indicate a change preliminary to fusion into colloid masses. The cells shown in Pl. VIII, Fig 1, are all taken from the adenoid layer of Case I. Fig. 1*c* shows a swollen cell containing large masses of colloid; the cytoplasm of the cell contains numerous fine melanin granules. There are a few smaller cells containing one or more colloid masses, some with, and some without pigment granules in the encircling rim of protoplasm. There are other pigmented cells,* mostly vacuolated, but without colloid contents (chromatophores, melanoblasts; see a paper read at the Lucerne Congress) both in and beneath the epithelial layer. All of these cells appear to be of essentially the same nature.

Compare with Fig. 1*c* the cell shown in Fig. 1*a*, from a section stained with ac. orceïn and polychrome methylene blue. Three small structureless spheres are seen, coloured only with the orceïn like the neighbouring colloid material, but they lie in clear spaces within the cell, differing thus decidedly from the condition in Fig. 1*c*. This cell, 1*a*, corresponds with the "Körperchenzellen," or phagocytes of lymph follicles. Fig. 1*b* shows a neighbouring similar cell, enclosing apparently a lymphocyte with nucleus darkly and uniformly coloured by methylene blue. One cannot say whether the small spheres of Fig. 1*a* are bits of colloid material that have been taken up by the cell or lymphocytes much altered by digestion.

In any case, the phagocytic cells 1*a* and *b* appear to have a different function from that of cell 1*c*, which presents no evidence of digestive action. Yet that the colloid substance in cell 1*c* has been taken up by the cell, and not formed within it, seems probable from the fairly clear distinction between colloid substance and the pigmented cytoplasm, and from the general absence of evidence of colloid degeneration within the other numerous cells present, plasma cells, etc. Here and there are scattered examples of cells such as

* The pigment is probably peculiar to dark- and yellow-skinned races, so far as colloid degeneration of the conjunctiva is concerned.

Fig. 1*d*, apparently swollen connective tissue or endothelial cells studded with clear vacuoles.

Fig. 1*c* is introduced for contrast with the above cells. It shows a plasma cell distended with hyalin refractile spheres ("Fuchsintropfen," Russell's bodies), coloured much more deeply with eosin than are the neighbouring colloid masses. There are only few such cells to be found.

The same homogeneous swelling and loss of specific staining affinities is found in colloid degeneration as in necrotic processes; and the colloid substance can perhaps scarcely be regarded as other than inert matter. In diphtheritic membrane fibrin, cells, and fibrous tissues all fuse into a uniform structureless mass containing only small refractile hyalin globules, which mostly stain with nuclear dyes. In the formation of colloid masses the evidence above given fails to indicate any very notable contributions from degenerating cells. In all of the four cases of colloid degeneration which I have seen the change was most advanced in the deeper tissues, where cells are not very plentiful.

B. Petrifaction and Ossification.

The bony spicules in Case II, found in some sections only, are in connection with a strip of fibrous tissue still remaining near the deep surface of the calcified mass; this fibrous tissue probably corresponds with the boundary of the tarsus, the colloid (and fibrous tissue) beyond being much more loosely arranged than in the main part of the mass. The mass, which, judging from the depth of colour obtained with hematoxylin, was unevenly impregnated with lime salts, is still penetrated by tracts of cells, such as those noted in Case I. Pervious blood-vessels are also fairly numerous, mostly widely dilated, with walls profoundly altered, in some cases only the endothelial lining remains, the rest of the vessel walls being merged in the surrounding homogeneous matter.

In the Trans. Oph. Soc., xxi, 1901 (q.v.), I reported a Case of Hypertrophy and Ossification of the Tarsus in a male Hindoo of 33 years.

Both upper tarsi were considerably enlarged upwards, the right one being partly ossified. In the left tarsus, which was only very moderately thickened, no abnormality was noticed in naked-eye appearance (on section) or in consistence or flexibility. The same applied to the unossified parts of the right tarsus. The apparent absence of colloid degeneration was supported by casual examination of sections of a small bit of the left tarsus excised. A recent examination, however, of these sections, and of small bits of the soft tissue attached to some of the bone removed from the right tarsus, shows unmistakable colloid degeneration, especially recognisable after re-staining with acid fuchsin and picric acid. There is homogeneous swelling of blood-vessel walls and of fibrous tissue bundles, breaking up of the latter, and fusion into blocks and masses, with loss of specific affinity for acid fuchsin. The deeper portion of the adenoid conjunctiva is also affected, but the change appears undoubtedly to have begun in the tarsus. This case is therefore closely related to the two now described, but the extensive ossification and considerable vertical enlargement of tarsus without macroscopic evidence of colloid change are extraordinary. The tests for amyloid were not applied. There was no extensive petrifaction as in Case II, reported above. The bony trabeculæ were firmly fixed in the apparently fibrous tarsus, and could not be removed without taking some of the soft tissue also.

In both the ossified cases the bony tissue is seen under the microscope to be at some points directly continuous with the neighbouring homogeneous degenerate tissue.

Description of Plates VII–VIII.

Plate VII, Fig. 1 (from Case I).—Cellular area extending deeply into tarsus. Disappearance of adenoid layer of conjunctiva to the right. Acid orceïn, polychrome meth. blue. × 120.

Fig. 2.—Much altered blood-vessel in subconjunctival tissues above the tarsus in Case II. Acid orceïn, polychrome meth. blue. × 120.

Plate VIII, Fig. 1.—Isolated cells in the adenoid layer of Case I. *a*, *b*, *c*, acid orceïn, polychrome meth. blue; *d*, *e*, hematoxylin and eosin. × 900.

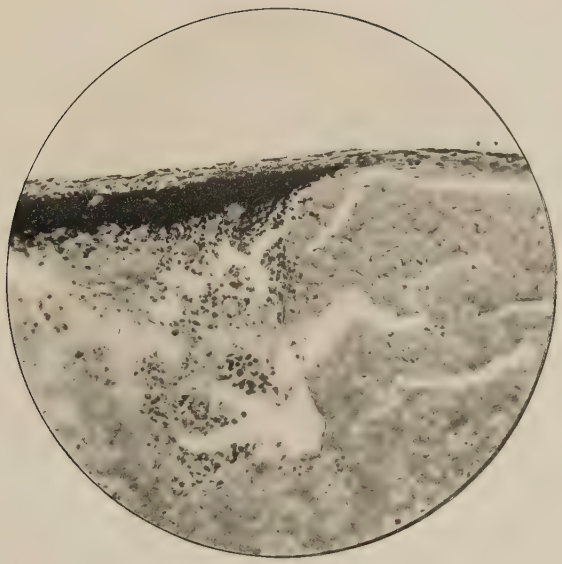

FIG. 1.

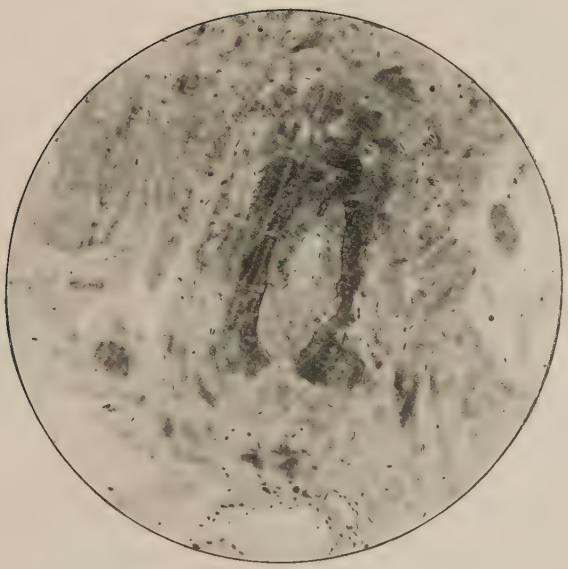

FIG. 2.

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A CASE OF GLIOMA RETINÆ IN A SHRUNKEN GLOBE.

By J. Herbert Parsons.

Edith Hopping, æt. 18 months, was admitted to the R.L.O.H. on 6.x.03, under Mr. Gunn.

The child had measles when 8 months old, pneumonia 6 weeks ago.

Family history good; 4 other children, no miscarriages; all the children have good sight.

The R. eye has been generally closed since recovery from pneumonia; it has been blind since measles. Convergent strabismus. Pain in head.

R. eye.—Globe shrunken, much injected.
Cornea hazy and infiltrated.
A.c. shallow.
Iris greenish-blue, vascular.
Lens ? opaque; fine vessels run on to capsule.
No reflex.
T –.

L. eye.—Not injected.
Cornea clear.
A.c. shallow.
Iris discoloured, vascular.
Yellowish-red reflex; vessels and hæmorrhages seen on surface.
Tn.

7.x.03. R. excision.

12.iii.04. Recurrence in R. orbit; protrusion of œdematous conjunctiva; elastic swelling felt. Child has been vomiting, and putting her hand up to the back of her head.

L. eye.—Cornea enlarged.
Iris discoloured.
Yellowish reflex behind clear lens.

6.iv.04. *R. eye.*—Contents of orbit protruding through palpebral aperture in fungating mass.

L. eye.—Marked proptosis, with fungating masses above and below.

Cornea dry and ulcerated.

8.iv.04. L. eye perforated and much more proptosed. Child very restless at night, and crying out almost continuously.

30.iv.04. Died.

Post-mortem Examination—head only examined.—Both orbits were full of gliomatous tissue, which also infiltrated and thickened the whole anterior part of the scalp and cranial bones. The chiasma was involved in a mass of growth. The roofs of the orbits were raised, so that the inferior surfaces of the frontal lobes were pitted, but not infiltrated.

Pathological Examination of the R. eye.—The R. eye was shrunken: antero-posterior diameter = 16 mm., transverse = 18 mm., vertical = 16 mm.

The eye was hardened in 10 per cent. formol, frozen, and bisected in a sagittal direction.

Macroscopic Examination.—Cornea very thick; a.c. absent; iris pushed forward; lens large, cataractous. Behind the lens is a yellowish-white mass, with reddish spots upon it; surrounding this mass is uveal pigment.

Microscopic Examination. Cornea.—Epithelium thin and ill-formed, surface level; it fills in the depressions formed by Bowman's membrane, which is very wavy. The condition very nearly resembles that depicted in my "Pathology of the Eye," vol. I, fig. 118, p. 182. Substantia propria much thickened, vascularised, and œdematous; the tissue is much spaced out, except in the anterior and posterior layers. The posterior surface of the cornea is thrown into large folds by the alteration in curvature produced by shrinking of the globe; rows of smaller sharp curves are superposed upon the large ones by wrinkling of Descemet's membrane. The endothelium is present only in places; there are microscopic deposits of pigment here and there, and some red corpuscles.

A.c.—Small and irregular.

Iris.—Transformed into a layer of fibrous tissue, with

horizontal long rod-shaped nuclei and patches of coal-black pigment scattered irregularly. It is adherent everywhere to the lens capsule.

Lens.—Cataractous. Ant. capsule thin, no cubical cells, only a few long rod-shaped nuclei. The lens substance, immediately beneath the capsule, is homogeneous. The whole of the central part of the lens is a sponge-work of broken-down fibres, granular coagula, etc. The posterior capsule is scarcely recognisable.

Ciliary Body.—Detached posteriorly ; much degenerated.

Choroid (*in situ*).—Congested and degenerated. It is irregular in thickness, compressed in places, pulled out into a spongy mass in others. The condition is that characteristic of phthisis bulbi.

Retina.—Not recognisable, except the pigment cells. Internal to the choroid is a layer of new-formed connective tissue of irregular thickness, but greater everywhere than that of the underlying choroid. The tissue is vascular and highly cellular, the cells being spindle-shaped and asteroid, with long nuclei. It is bounded on the outer side by nearly continuous coal-black retinal pigment epithelium, which in places spreads inwards in intertwining tubules and bands.

The whole of the vitreous cavity is filled with granular material, staining with eosin. At first glance it resembles an ordinary albuminous coagulum. On minute inspection it is found to consist of degenerated cells. In a few places round nuclei, still staining with hæmatoxylin, are seen in groups, and one or two of these groups have calcareous deposits. Around the periphery there is extensive extravasation of blood.

This tissue is, I think, undoubtedly cellular, but necrotic. As far as can be made out the cells have no resemblance to leucocytes ; nor are they of connective tissue origin. They do not bear much resemblance to glioma cells, but are more like the cells in the degenerated parts of gliomata than any others. They resemble the cells found in other cases of glioma in shrunken globes, some of which I have been able to compare with them.

The optic nerve is atrophic, but highly cellular. The cell nuclei vary greatly : most are oval and faintly staining, probably

neuroglial; others are rod-shaped and deeply staining, undoubtedly of connective tissue origin; others are small, round, and deeply staining, probably gliomatous, but it is impossible to be certain of this point.

Microscopical examination of portions of the orbital and intra-cranial extensions showed the typical features of glioma retinæ as it occurs in extrabulbar extensions, *i.e.*, with exuberant growth and none of the characteristic degenerative patches.

This case is of great importance as an almost incontestable case of glioma of the retina in a shrunken eye. There is only one point about the clinical history which renders causal association between the glioma and the phthisis bulbi open to doubt, viz., the fact that the blindness of the eye dates from an attack of measles at the age of 8 months, or 16 months before the child came under observation. The phthisis may have been due to shrinkage following perforation. On the other hand it is impossible to explain the peculiar degenerated cells in the vitreous on inflammatory grounds. They are indeed not characteristic of glioma, though they resemble glioma cells more than any others. Apart from the subsequent history of the case their exact nature must have remained obscure, and indeed, when I examined the eye shortly after removal, I was unable to arrive at a more definite conclusion than that the cells were probably gliomatous. In support of this diagnosis is the fact that such extensive growth of glioma in the right orbit as was discovered at the *post-mortem* examination would be unlikely from mere extension from the opposite orbit *viâ* the chiasma. Where both eyes are affected in glioma—a not inconsiderable class (about one-fourth of all the cases)—the second eye is not affected by extension *viâ* the chiasma, but is the seat of an independent growth. I have had the opportunity of examining the sections of two of the reported cases of glioma in a shrunken globe—those reported by Treacher Collins and Marshall. The cells which were regarded as gliomatous in these cases exactly resemble those

found in this case, and, as far as the nature of these cells is concerned, there is no more reason for regarding them as gliomatous in one case than in another; in no case yet reported are they absolutely typical.

I have collected from the literature 14 cases of glioma of the retina associated with shrunken globe, so that there are now 15 cases on record. The principal points of interest in these cases are briefly set out in the table appended. It is unnecessary to enter into further detail since the most important have been published in English and are readily accessible.

It will be noticed that in no less than 10 of the cases it is stated that the other eye was the seat of glioma, in another case this eye was blind, whilst in the remaining 4 the condition of the other eye is not stated, so that it may be safely concluded that it was normal. In several of the cases there is no doubt that the eye became perforated before the onset of the shrinking, usually as the result of extra-ocular extension of the growth. In the other cases it is almost impossible to decide whether perforation occurred or not; it is a difficult point to settle in a shrunken eye on pathological examination alone. There have often been inflammatory symptoms preceding the phthisis bulbi, and it is probable that the shrinking is due to this rather than to any inherent tendancy in the growth itself (Brailey), comparable with atrophic scirrhus; such an occurrence must be so rare as to almost negative the hypothesis. I am still of the opinion that the gliomatous nature of the cells in these shrunken eyes is not placed absolutely beyond cavil. It is, however, of the utmost importance that all similar cases should be carefully investigated and put on record.

There is a cognate question which is of considerable interest, viz., temporary retrogression in glioma retinæ. Such cases appear most frequently in the earliest reports, probably owing to the fact that the need for immediate operation was not recognised (Wintersteiner). Almost invariably the tumour commenced to grow again rapidly at a later date,

Case.	Author.	Sex.	Age.	Eye.	Other eye.	Duration of disease.	Clinical condition.
1	Sichel ..	?	3	R.	Glioma ..	..	Amaurotic cat's eye ..
2	Knapp ..	M.	$1\frac{3}{4}$	R.	? ..	8 days ..	Inflammation; protrusion; perforation; second perforation in 3 months; shrinking
3	Hirschberg and Happe	F.	20 weeks	R.	Glioma ..	20 weeks ..	Hyphæma; shrunken globe
4	Wadsworth	M.	14 months	L.	Blindness	8 months	Inflammation; swelling, then shrinking
5	Armaignac..	F.	26 months	R.	?	10 „	Shrunken globe; perforation
6	Snell ..	?	21 months	R.	Glioma ..	3 „	Shrunken globe .. ..
7	Brailey ..	F.	9 months	L.	„ ..	..	Painful; shrinking; hyphæma
8	Brailey ..	F.	26 months	R.	„ ..	10 months	Panophthalmitis; shrinking
9	Lawford and Collins	M.	9 months	L.	„ ..	..	Shrunken globe .. ..
10	Lawford and Collins	M.	2	L.	„ ..	..	„ .. ..
11	Collins ..	M.	16 months	L.	„ ..	15 months	„ .. ..
12	Lukowics ..	M.	18 months	L.	..	15 „	Varied in size; perforation
13	Marshall ..	F.	5	R.	Glioma ..	4 years 9 months	Glioma; in 3 years and 9 months shrinking
14	Lagrange ..	F.	7	L.	..	18 months	Inflammation and shrinking
15	Parsons ..	F.	18 months	R.	Glioma ..	10 „	Shrunken globe .. ..

Operation.	Result.	Macroscopic examination.	Microscopic examination.
Nil	Marasmus. Death ..	White tumour of retina. Optic nerve normal	Nil.
Enucleation ..	Recurrence (extirpated). Death	Red mass with hæmorrhage ..	Glioma.
„ ..	No recurrence. Death	Growth on nasal side anteriorly	„
„ ..	Recurrence. Death ..	Filled with growth. Extra-ocular growths. Optic nerve enlarged	
„ ..	„ „ ..	Large growth in orbit	
„ ..	Death	"Undoubtedly glioma"	
„ ..	.. ..	Thickened detached retina ..	? Glioma.
.. ..	Growth in L. and metastases.		
Enucleation ..	?	Shrunken globe; choroidal inflammation; infiltration (? inflammatory) of nerve	„
R. eye enucleated	?	Not examined.	
Both enucleated ..	.. ..	Full of grey substance. Lens absent	"Typically gliomatous."
Exenteration ..	No recurrence in 3½ months	Globe full of tumour	Glioma.
Both enucleated ..	.. ..	White mass in vitreous ..	„
Enucleated ..	No recurrence in 2 years	Filled with growth	„
„ ..	Death	White mass in vitreous ..	„

and the few cases in which this did not occur may be reasonably considered to have been errors in diagnosis. The difficulties in the differential diagnosis of glioma from pseudogliomata of various kinds are often so great as to be insuperable. Many of these cases show temporary diminution of intra-ocular tension and distinct tendency to shrink, without, however, going on to complete atrophy of the globe. They, therefore, represent a group very nearly allied to the cases under discussion, and are of great importance in demonstrating that quite undoubted gliomata may show signs of shrinking at some stage of their history.

Including the cases of complete phthisis bulbi, Lagrange has collected 21 cases which showed temporary retrogression. The cases reported by Tyrrell, Rolland, Knapp and Grolmann are particularly interesting in that they showed alternate tendencies to shrink and to grow. The most striking is Grolmann's case. Here, a child of 6 had had the right eye removed for glioma 4 years previously. The left then showed a grey reflex ; no vessels could be seen. After 2 days' treatment with inunctions the mass diminished in size, and in 17 days it could only be seen with the pupil dilated. Five weeks later numerous yellow nodules were seen floating in the vitreous, and 2 months afterwards the tumour commenced to grow, accompanied by inflammatory symptoms. Hypopyon appeared, which was repeatedly evacuated, but recurred. The growth increased until it reached the lens, glaucoma setting in ; then the cornea became ectatic. Finally the tumour filled the anterior chamber, perforated the cornea, and grew rapidly outside the globe. In about a month the child died, the disease having lasted in this eye for 11 months. It will be noticed that this eye never shrank.

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A CASE OF (?) TUBERCLE OF THE RETINA.

By W. Ilbert Hancock, F.R.C.S.

A. J., æt. 19, was first seen in November, 1901, complaining of failure of vision in the right eye. The failure, gradual in onset, had extended over a period of about 8 months, but had of late increased somewhat more rapidly, which the patient attributed to an attack of mumps 6 weeks before. The youth, a farm labourer, was apparently in robust health. Careful enquiry into his family and personal history elicited nothing of importance, and Dr. Wood who kindly examined the patient reported that he could find no evidence whatever of organic disease.

Right eye, V. = counts fingers, not improved with glasses. Divergent strabismus 15°, no pain or injection. No k.p. Tn. Lens clear. Ophthalmoscopic examination showed a large yellowish-white area, situated on the temporal side of the disc and extending over the macular region (Pl. VIII, Fig. 2). The patch was roughly square in shape, the sides being equal to about 2 disc diameter, and the surface was best seen with + 5 D; the patient being emmetropic, it was, therefore, raised about $1\frac{1}{2}$ mm. Its outline was fluffy and ill defined; skirting it above and below were the superior and inferior temporal vessels respectively, the veins large and tortuous, being here and there partially obscured by retinal œdema. A few small whitish ill-defined areas were arranged immediately below and to the outer side. Two small macular arteries coursing horizontally outwards from the disc were almost at once lost to view, disappearing in the affected area. The disc, though not involved, was blurred in the temporal half and the veins were full, but there was no swelling. No hæmorrhages, new vessels, or abnormal pigmentation could be made out either on the patch itself or elsewhere in the fundus. Vitreous clear. Left eye V. = 6/6 J. 1. Fundus normal.

The patient was ordered potassium iodide and advised to return in six weeks. At the end of that time the affected area was found to have considerably increased in extent, it was then encroaching upon the nerve-head above and to the outer side. The surgeon under whose charge the patient came, recognising the gravity of the condition, the great impairment of the eye as a seeing organ, and the possibility of its being either malignant or tubercular, advised excision.

The enucleated eye-ball having been hardened in formol, frozen and bisected, was first subjected to a careful macroscopic examination. The vitreous, which was quite clear, was found to be abnormally adherent to the surface of the patch, tearing away from it with difficulty. The retina remained *in situ*, but on subsequently passing the eye through spirit it became detached, and it was at once seen that the morbid focus was entirely confined to the retina, the choroid and overlying pigment epithelial layer both to the naked eye and examination with the corneal loupe appearing quite normal. After embedding, colloidin sections were cut, which showed the following characteristics:—

The retina is thrown into numerous folds and separated from the choroid by a narrow band of exudation staining deeply with eosin (Pl. IX). The choroid is normal in appearance, the membrane of Bruch intact and covered by an apparently unaltered layer of hexagonal pigment epithelium. In the thickened folded retina are two well-defined plaques of granulation tissue; these in the majority of the sections are seen to be quite distinctly separated from one another by retinal layers which, though quite recognisable, have undergone more or less change, but in a few sections they are seen to be connected by a band of fibrous tissue which, as it were, perforates the intervening retinal layers (Pl. X, Fig. 1). The anterior or internal plaque, confined to the nerve fibre layer, is chiefly composed of ill-developed fibrous tissue containing well-marked giant cells, and exhibits extensive round celled infiltration (Pl. X, Fig. 2). The giant cells are of the large branching type with well-defined nuclei

arranged without exception in the centre of the cell. The small celled infiltration is especially evident in the perivascular lymph spaces and bears no definite relation to the giant cells, nor are the latter surrounded by any epithelioid cells as in typical tubercular systems.

The posterior or external plaque, confined, to the rod and cone and external nuclear layers, is also chiefly made up of cellular fibrous tissue, but differs markedly from the anterior in containing a large number of blood vessels and proliferated pigment epithelium, and there is an entire absence of giant cells. The whole affected area is sharply limited, passing abruptly into œdematous but otherwise normal retinal tissue. No tubercle bacilli could be demonstrated. Whether the anterior or the posterior plaque was the primary seat of the lesion it seems impossible to determine. The cornea, iris, lens, ciliary body and optic nerve were normal.

The above sections show that we are obviously dealing with some chronic inflammatory change in the retina, and the question arises as to its causation. Syphilis may, I think, be definitely excluded, there being no evidence of the inherited or acquired form of the disease, and the patient denied most emphatically ever having exposed himself to infection. This being so, one naturally asks is it tubercular? The patient's family history throws no light on the subject. His father died at the age of 76, of senile decay; his mother is alive and well, and his only sister enjoys excellent health. There have been no other children, and as far as could be ascertained, there is no history of tubercular disease either on the paternal or maternal side of the family. We have, therefore, to form an opinion on the histological characteristics alone.

The presence of giant cells in the anterior plaque would lend weight to the tubercular origin of the growth, but at the same time it must be admitted that the character of these cells is not that generally associated with tubercle nor, as mentioned above, is there any sign of tubercular systems. On the other hand, it is generally recognised that the

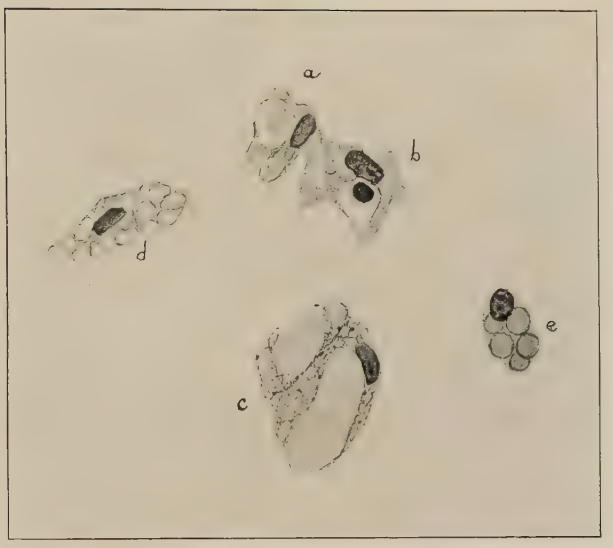

FIG. 1.

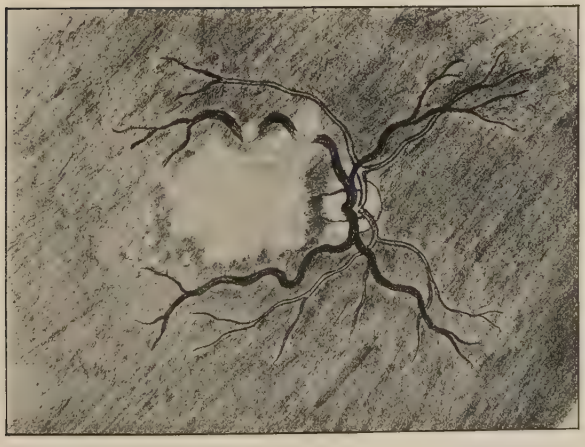

FIG. 2.

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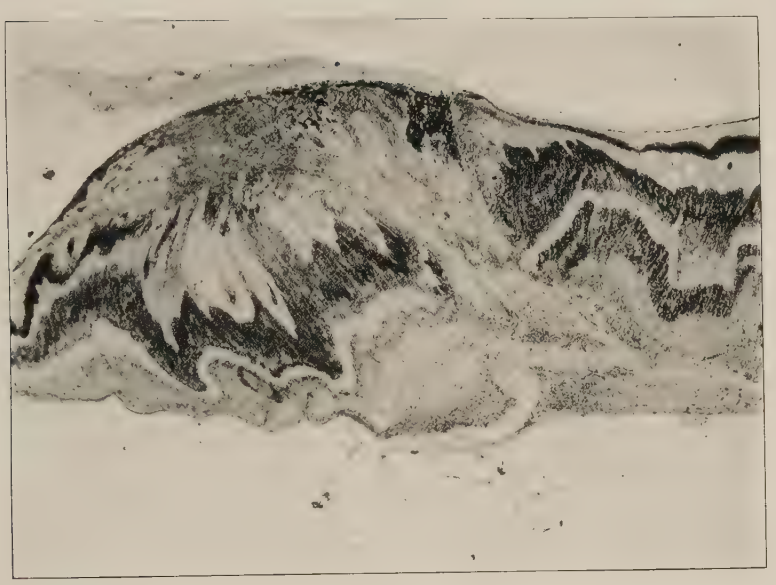

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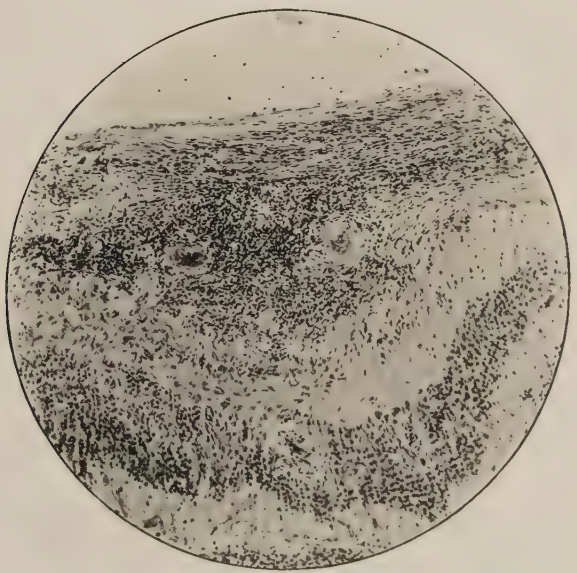

FIG. 2.

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histological characteristics of tubercular lesions are extremely variable, and that there are but two ways of positively asserting a lesion to be of that nature. Firstly by inoculation experiments, which were obviously impossible in this particular case. Secondly, by the demonstration of the specific organism. This latter is a purely positive test and the eye-ball having been hardened in formol would render the demonstration of the tubercle bacilli, even if present, extremely uncertain. It seems, therefore, reasonable to look upon the case as one of retinal tuberculosis, until further information on this class of case is forthcoming.

The case is also interesting in that it is an example of a not uncommon class met with clinically, that of the large solitary patch of inflammation situated, as a rule, in the vicinity of the disc, especially in the macular region, and which we have so seldom an opportunity of examining microscopically.

Careful search through ophthalmic literature has resulted in my finding several references to the subject of retinal tuberculosis. O'Sullivan and Story publish an extremely interesting case of the condition, confined to the internal retinal layers and commencing in the immediate vicinity of the disc. This seems to be the first recorded case of the disease which has been diagnosed clinically, and subsequently verified by microscopic examination. In this case there was no evidence of tuberculosis in any other part of the body, but as the authors rightly point out, it is of course difficult to exclude this possibility.

Ginsberg speaks of it as being invariably secondary to tubercle of some other part of the eye, *e.g.*, iris, ciliary body, or choroid, and indeed it is not uncommon, especially in the latter condition, to find isolated foci of the disease in the retina. Tubercle of the optic nerve with or without implication of the retina, has been described in a few cases, notably by Bongartz, Demours, Cruveilhier, Wagenmann and Sattler, but in all these cases there was evidence of a similar disease in some other part of the body.

Schöbl, Bach, Perls and Manfredi, all speak of retinal tuberculosis, but these cases are obviously secondary to implication of some part of the uveal tract.

In conclusion my best thanks are due to Mr. Richardson Cross for his kind permission to publish the case, and also to Mr. W. T. Lister for the admirable micro-photographs which serve to illustrate this paper.

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Description of Plates VIII–X.

Plate VIII, Fig. 2.—From a rough pencil sketch of the fundus made on the patient's first visit to show the position and extent of the affected area.

Plate IX.—Section showing the folding of the retina and the anterior and posterior plaques separated from one another by easily traceable retinal layers.

Plate X, Fig. 1.—Section of retina showing the anterior and posterior plaques connected by a fibrous strand which perforates the intervening retinal layers.

Fig. 2.—The anterior plaque of the section in Pl. IX, under a high power, showing the giant cells and small cell infiltration.

INTRADURAL TUMOUR OF THE OPTIC NERVE. NEURO-FIBROMATOSIS.

By M. S. Mayou.

(From the Andrew Clark Laboratories, London Hospital.)

Intradural tumours of the optic nerve are not common, although not exactly rare.

F. Lagrange[1] has collected some 173 cases: Byers,[2] 102 cases; Lawson,[3] Treacher Collins, Marshall[4] and Werner[5] have published some cases in this country, Lagrange, Byers, and Werner having reviewed the subject as a whole.

The object, therefore, of describing this case is that the tumour was removed when comparatively small, and it shows well the distribution of the nerve fibres and the origin of the tumour.

L.J., female, æt. 5, attended Moorfields on March 9th, 1904, complaining of right convergent strabismus. At the same time it was noted that the right eye was apparently smaller than the left, which was probably due in reality to a slight proptosis in the left eye. Her refraction was estimated by retinoscopy, and was

Rt.	Lt.
+3 / +3	+6 / +6

On July 25th, 1904, the patient came under my observation at the London Hospital whilst I was doing Mr. Lister's work.

There was a history of slowly increasing proptosis, noticed first in December, 1903, with loss of vision in the left eye. There was no pain, and otherwise the child seemed a strong healthy girl, apart from some adenoids with secondary deafness.

The proptosis was not great in amount and the lids could be easily closed over the globe. The eye was pushed straight forward.

The movements of the globe were not limited.

No tumour could be felt, no pulsation or bruit distinguished.

The globe was not congested. The pupil was inactive to light but reacted consensually.

Media, clear.

The fundus showed well-marked optic atrophy. The edges of the disc were somewhat blurred and a small amount of exudation could be seen along the vessels.

The arteries were small but the veins were considerably enlarged.

V.L. no P of L.

By retinoscopy I estimated the refraction as $-\frac{+7{\cdot}5}{+7{\cdot}5}$ in the left eye; that is to say, there had been an increase in the hypermetropia. On this point the gentleman who performed the original retinoscopy did not agree.

On July 28th, 1904, a vertical incision was made along the outer wall of the orbit to the bone. The periosteum was then stripped up from the inner surface of the orbit and incised. On passing the finger behind the globe a hard rounded tumour could be felt, wedged into the apex of the orbit. Horizontal incisions were carried outwards from the upper and lower end of the original incision, reaching down to the bone. The outer bony wall of the orbit was then sawn through above and below into the spheno-maxillary fissure, and the flap together with the bone turned outwards. Although this gave ready access to the tumour the posterior part of it could not be seen. There was at least $\frac{1}{2}$ cm. of free nerve between the globe and the tumour. Keeping as close to the tumour as possible a pair of curved scissors were passed behind the tumour from the outer side and the nerve divided as close to the optic foramen as possible. It was then freed in front by dividing the nerve close to the globe. The flap was replaced and sutured in position by skin stitches. No drain was put in the wound. The wound healed by first intention and the sutures were removed on the 4th day. Some trouble was given by the enormous proptosis which was present for some days after the operation, and indeed a small ulcer formed on the lower part of the cornea, which subsequently healed.

On August 24th the patient was discharged from the hospital.

At that time there was complete ptosis although the lid could be slightly raised. The cornea was anæsthetic and the movements of the globe were nil. The fundus was difficult to make out as there was some opacity in the media. It was pale, but the vessels could still be seen.

On October 26th the eyelids could be raised to a slight extent. The vessels of the bulbar conjunctiva were dilated. The globe showed some movement and there was slight enophthalmos; the pupil was widely dilated, and there was some return of sensation to the bulbar conjunctiva. The cornea was hazy below, owing to the pressure of the lid margins and the nebula left by the old ulcer.* The pupil did not react consensually.

Fundus.—The area of the disc was occupied by a mass of white exudation which protruded forwards to a slight extent into the vitreous, the exudation extending into the retina along the vessels. At the edges of the upper part of the mass of exudation the retinal vessels could be recognised, especially the veins, which were very full. These vessels contained blood, but it was impossible to determine the direction of the blood-stream in them. Further out, beyond the exudation, there was some disturbance in the choroidal pigment.

Morbid Anatomy.—The tumour measured 2·5 cm. long and 1·8 vertically. It was fusiform in shape, the diameter of the optic nerve at the cranial end measuring double that in front of the tumour. It was situated entirely within the dural sheath. Spread out over the surface and more or less incorporated with it were the long ciliary nerves together with the ophthalmic artery. Near its posterior part was a small portion of a nerve of larger calibre which was probably a portion of the third nerve. As the tumour was jammed into the apex of the orbit the cutting of these was unavoidable. The tumour was hardened in formol for 24 hours and divided longitudinally. On section it was white in colour and not very vascular. The central artery of the retina was present in it and there was some softening and hæmorrhage near its centre. Portions of the tumour were embedded in paraffin and subsequently stained with logwood and

* Since this date a small trophic ulcer has formed in this situation.

eosin; others were put into Muller and Muller and osmic acid and preparations made by Marchi's and by Weigert's methods.

Microscopic sections showed that the tumour was completely encapsuled by the sheath of the dura mater, which was not infiltrated by the tumour. In front of the tumour this sheath was considerably distended, and this, with the pressure of the tumour on the central vein, no doubt accounted for the optic neuritis which had been present. The tumour consisted of two portions: the lower, through which the optic nerve ran, and the upper, which did not contain any part of the optic nerve. Separating these two was a fine membrane which seemed to be derived from the pial sheath, through which I think the upper part of the tumour had spread. The upper part of the tumour consisted of cells of the type found in the trabecula of the optic nerve and enclosing spaces which I think were attempts at reproduction of the spaces found in that structure for the nerve bundles. All these spaces were very irregularly arranged. In the lower part of the tumour where the nerve was present there were no spaces, the increase of interstitial tissue being arranged longitudinally between the nerve fibres, each individual nerve fibre being widely separated from any other. Where the nerve was cut through posteriorly the interstitial tissue was considerably increased, although there were no irregularly arranged spaces as seen in the upper part of the tumour, there being simply a general increase in the neurilemma. The optic nerve close to the globe was free from any increase in interstitial tissue and was of about its usual calibre, the fibres staining well by Weigert's method. As the nerve passed backwards the fibres showed by their absence most degenerative changes in two situations:—

(*a*) In the upper part of the nerve, just before entering the tumour; that is to say, at the point where kinking of the nerve took place by the movement of the globe in front of the tumour.

(*b*) In the upper part of the nerve, within the tumour, at the point of its greatest diameter, where most separation of the nerve fibres had taken place.

The nerve fibres themselves showed very marked beading and wavy outline, partly, no doubt, due to degeneration, but partly due

to technique, as the tumour was not pinned out while being hardened. In some situations actual rupture of the nerve fibres seems to have taken place. Although Marchi's method was followed with every care, on two separate portions of the tumour no staining of the myelin sheath could be made out. This, perhaps, is accounted for, since the tumour must have existed at least 7 months, and therefore the destruction have been very slow and the material staining by Marchi's method absorbed.* No axis cylinders could be made out in the logwood and eosin sections.

The cytoplasm of the cells was very ill defined. The nuclei are of two types; one the large oval elongated faintly staining nucleus resembling those of endothelial cells, and the second a small rounded darkly staining nucleus. The cells are not undergoing mitosis to any extent; only one cell in the aster stage could be found in section after examining under a $\frac{1}{12}$th for an hour. The type of mitosis in this cell could not be made out.

The blood vessels in the tumour were extremely scanty, but where present were well formed and usually had both endothelial and perithelial coverings.

Conclusions.

The *Etiology* of this case, taking Byers' statistics, is very typical.

The *age* was 5 years. Six-eighths of the cases appear before the age of 15 and five-eighths before the age of 10.

Sex.—The patient was a girl. The female sex provides 59 per cent. of the recorded cases.

Side.—The left side is more frequently affected than the right, 55 per cent. It was the left side which was affected in this patient.

Symptoms and Clinical Appearance.—Failing vision with a painless proptosis, the eye being pushed straight forward with very little limitation of movement; secondary optic

* Degeneration changes have not been shown to occur in neuro-fibromata of the spinal nerves, although motor paralysis has been recorded (A. Thompson[6])

atrophy with distended veins, and increasing hypermetropia are all cardinal signs which were present in this case.

Pathological Anatomy.—The condition was one of neuro-fibromatosis of the optic nerve. The irregular fusiform shape of these tumours seems fairly constant and, as in this case, usually affects the part of the optic nerve at the back of the orbit. It is extremely probable that the diffuse enlargement of the nerve extended within the skull as there was a great increase of interstitial tissue which extended right up to the optic foramen, although in this situation there was no overgrowth outside the nerve proper. That this thickening does occur within the skull has been shown by Byers in 11 cases which he has collected, all of which, with the exception of 2, died from meningitis after operation. One of the others died of pulmonary tuberculosis, and in one of Byers' own cases death was due to the actual growth of the tumour within the skull.

The localised swelling, which was external to the nerve proper, was identical in structure with the nerve sheath, the spaces found in it being attempts at the reproduction of the spaces for the nerve bundles, the condition, therefore, being a general increase of interstitial tissue with a localised over-growth outside the nerve. Presumably owing to the presence of these spaces some of these tumours have been called lymph-angiectasis fibroma, but, as has already been pointed out, these spaces are not lined by endothelium but are lined by the actual cells of the tumour. It is probable that most of the recorded cases belong to this type, the great variety of names which have been given to them being due to secondary degenerative changes in the tumour. Thus myxo-fibroma has been applied to those cases in which the spaces have become distended with a homogeneous coagulum.

Although it is probable that myxo-sarcomata do occur, many of these tumours have been described as malignant on insufficient data: namely, the occurence of other tumours along the course of the same or other nerves; unless there is infiltration of the orbital tissue with the growth, or

secondary growths apart from nerve tissue occur, or unless possibly the type of mytosis in the cells can be demonstrated, it is not correct to call these tumours malignant. Endotheliomata undoubtedly occur within the nerve sheath but form an entirely different type of tumour from the neuro-fibromata.

The destruction of the nerve fibres in my case was most evident in two situations:—

(*a*) In the central part of the tumour; that is to say where the pressure is greatest, and

(*b*) At the point where the nerve passes into the tumour in front; especially is this evident in the upper part of the nerve. This seems to be undoubtedly due to the kinking of the nerve at its junction with the swelling.

It is probable that some destruction of nerve fibres is also produced by the fibrosis following the optic neuritis, although there was not much evidence of this, as these myelin sheaths directly behind the disc took up the stain readily. The destruction of the fibres seems to be comparatively slow, since staining by Marchi's method showed no changes in the myelin sheath; probably this was due to the absorption of the material staining by this method.

The cause of the optic neuritis is obviously due to the distension of the nerve sheath between the tumour and the globe, probably secondary to pressure on the central vein which was involved in the tumour and was engorged both within (ophthalmoscope), and behind the globe. The secondary optic atrophy is more difficult to explain, the chief factors in its production being fibrosis together with the dilatation of the communicating veins between the central vein and the veins of the nerve sheath.

The regurgitation of blood into the retinal and choroidal vessels after division of both the main ophthalmic artery and the central artery is of considerable interest; unfortunately owing to the condition of the media the earliest stages could

not be observed, but, as has been shown by Knapp[7] and Parsons[8], after division of the central vessels the distal end becomes occluded and blood finds its way back into the vessels from the perforating branches of the anterior ciliary vessels. The ophthalmic artery in this case was divided near the foramen; although it is possible that some muscular branches may have escaped, the conjunctival congestion which persisted was suggestive that in this case an additional source of supply was the anastamosis between the anterior ciliary and the posterior conjunctival vessels and so back to the perforating arteries.

The return of sensation to the conjunctiva and of the motor power to the muscles were probably dependent on the regeneration of the nerves, the exact method of which is as yet to be demonstrated.

In conclusion I have to thank Mr. Herbert Parsons for the use of the hospital camera and for the assistance he has given me in taking the microphotographs which illustrate this paper.

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Description of Plates XI–XIV.

Plate XI, Fig. 1.—Full face view of L. J., showing proptosis of the left eye.

Fig. 2.—Tumour after removal, showing the ciliary nerves and ophthalmic artery adherent to the capsule.

Plate XII, Fig. 1.—Longitudinal section of the tumour (Weigert, Pal.). Note the lower part of the tumour contains nerve fibres; also the difference in size of the nerve anteriorly and posteriorly. There has been some hæmorrhage near the centre of the tumour.

FIG. 1.

FIG. 2.

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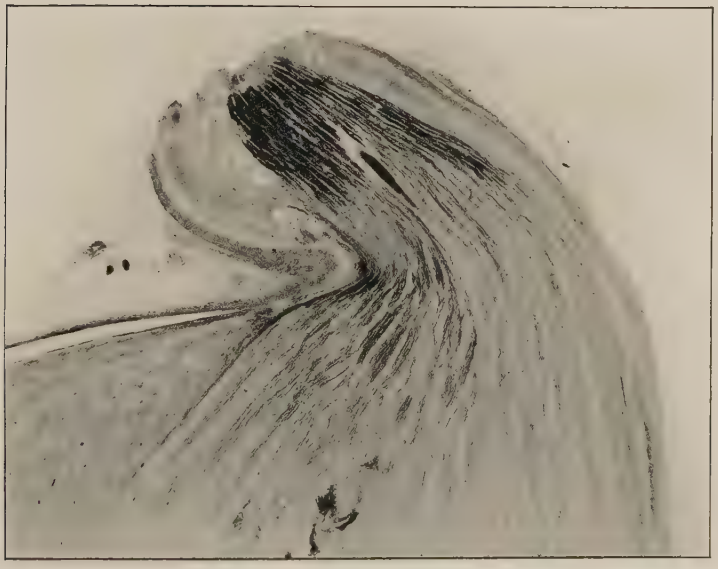
FIG. 1.



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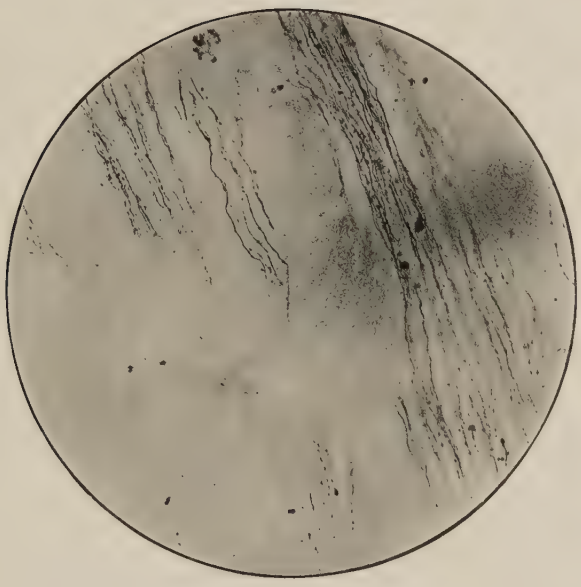

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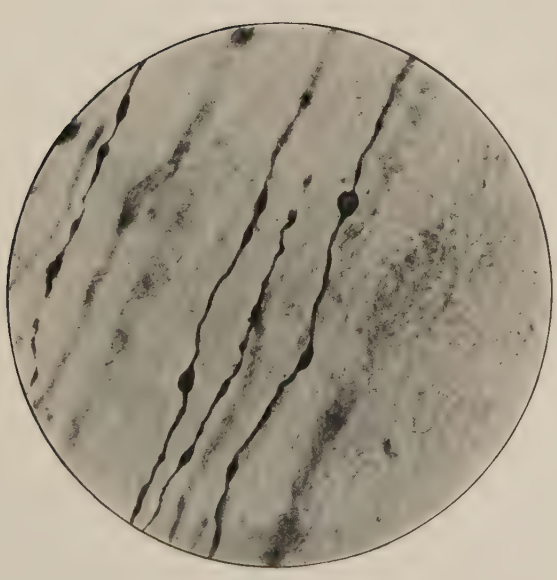

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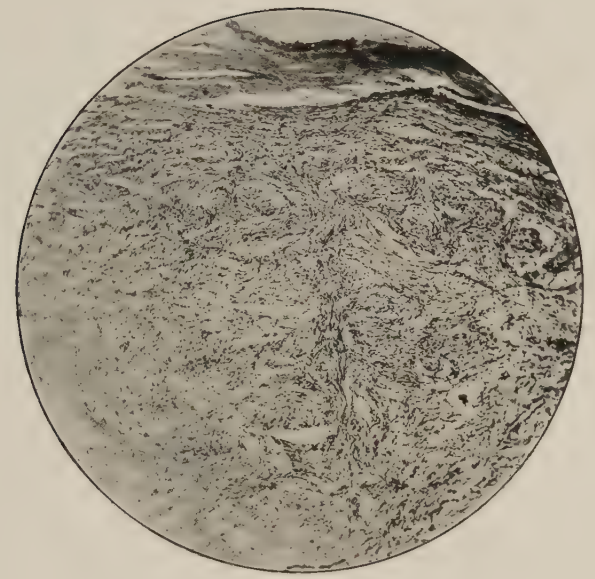

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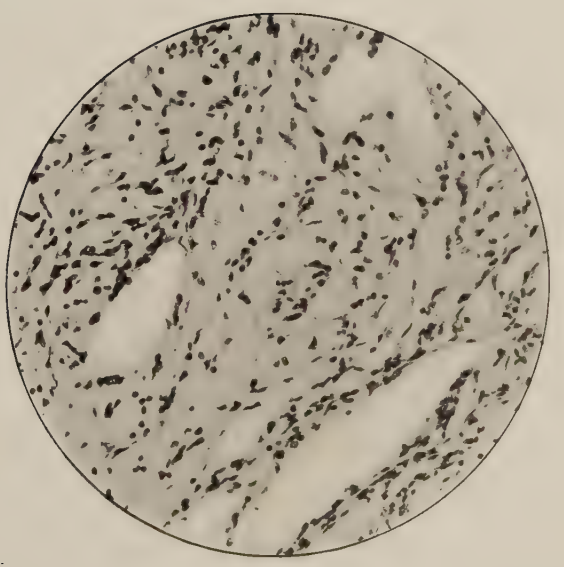

FIG. 2.

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Plate XII, Fig. 2.—The anterior end of the nerve and tumour (Weigert—Pal.). Note (*a*) the distension of the nerve sheath in front of the tumour; (*b*) the degeneration in the upper part of the nerve produced by the kinking; (*c*) the process of the pial sheath passing between the upper and lower portions of the tumour; (*d*) the separation of the nerve bundles by interstitial tissue.

Plate XIII, Figs. 1 and 2.—Showing the separation of the nerve fibres by interstitial tissue (Weigert—Pal.). Fig. 1 also shows a nerve bundle which has probably ruptured. Fig. 2, beading of the nerve fibres.

Plate XIV, Fig. 1.—Upper portion of the growth, showing the trabecula spaces. In the upper part of the section can be seen the dural and arachnoid sheath. (Logwood and eosin.)

Fig. 2.—High-power view of the same. Note the spaces are lined by the cells of the tumour. (Logwood and eosin.)

THE STRUCTURE OF THE MEMBRANE OF BRUCH, AND ITS RELATION TO THE FORMATION OF COLLOID EXCRESCENCES.

By George Coats.

(From the Pathological Laboratory.)

The histological details of "colloid excrescences" of the membrane of Bruch have been tolerably fully worked out. We know that they appear first as small homogeneous or slightly granular bodies underneath the pigment epithelium in close connection with the membrane of Bruch, and that they grow either singly or by coalescence in the form of little nodular masses. Only when they have reached some size do they lose their homogeneous structure and undergo various secondary changes, *e.g.*, lamination, disintegration of their centres, calcification, formation of a central core of connective tissue (probably by invasion), and, finally, bone formation from ossification of the invading connective tissue. So much is well known and universally admitted; when, however, we come to the explanation of the origin of these bodies, we meet with considerable diversity of opinion, in spite of the very large amount of work which has been done on the subject.

Certain theories may be put aside as discredited or inherently improbable, such as Rudnew's, that they arise from hyaline degeneration of wandering leucocytes, and Pes's, that they may arise by processes of sclerosis and atrophy in superficial papillæ of the choroid formed in consequence of the cicatricial contraction following upon inflammation in the middle and deep layers of that tunic. The theory of Hofmann also may be merely mentioned; this author states that they arise from hyaline degeneration of thrombi in the choriocapillaris vessels, or of the endothelial cells lining their walls. The hyaline masses so

formed project in their growth against the membrane of Bruch, and finally rupture it and pass through to the inner side, after which, so says Hofmann, the membrane heals up again, and thus is produced an appearance as if the membrane of Bruch ran past the excrescence unchanged. This appearance undoubtedly occurs (see Pl. XV, Fig. 4), and has been the cause of much of the controversy, since it has led many to deny to the bodies any connection histologically or developmentally with the membrane of Bruch. I shall discuss the point later.*

No one who has examined many of these excrescences will be inclined to consider these three theories when he notes how strictly the bodies are confined to the inner layers, and how they not infrequently occur in choroids quite free from all traces of inflammation, past or present. Leaving these explanations, therefore, out of consideration, opinions will be found to be divided into two main camps: (1) The excrescences arise from actual transformation of the cells of the pigment epithelium. (2) They arise, as the membrane itself is supposed to arise, as a deposit from the cells of the pigment epithelium, but without actual transformation of pigment cell into excrescence. The former of these may be conveniently referred to as the "transformation" theory, the latter as the "deposition" theory.

The transformation theory, which was first enunciated by Donders, has, perhaps, the most supporters, and seems to be favoured by recent investigators, at least in Germany.† The details of the process are variously given by different authors. Donders believed that the nucleus became hyaloid, and so formed a minute excrescence, but it was afterwards pointed out (by de Vicentiis) that it was more consonant with general pathological principles that the protoplasm

* It should be stated that Hofmann, arguing from this supposed origin, believes that the bodies described by him are not ordinary colloid excrescences, but neither in his description nor in his figures can any warrant be found for placing them in any other class.

† An historical review, with references to literature, will be found at the end of this paper.

should be first affected by a degenerative process. Since the colloid bodies were found mostly in the eyes of old people, it was natural to connect them in origin with the well-known senile changes in the epithelium. It was, therefore, explained that the pigment epithelium became irregular in its arrangement, some of the cells being larger than others and sometimes containing two nuclei; the layer might also be doubled. In addition the pigment was irregularly distributed, denser in some places and thinner in others, while the little rods normally found were replaced by round granules. Certain of these pale cells became more and more homogeneous, lost their nuclear staining, and finally became converted into small colloid bodies which grew by accretion. Or, according to others (*e.g.*, Dimmer), colloid globules appeared within the cell-protoplasm which, becoming larger by confluence, finally destroyed the cell and formed a minute colloid body, the larger being the result of the fusion of many smaller.

There are many difficulties in accepting this theory of origin. In the first place the histological appearances do not support it, for in an early stage the bodies, if stained in the usual manner with eosin, have the appearance of being thickenings of the membrane itself, provided that the section passes through their middle (see Fig. 3). They seem, however, early to form a knob-like head, and if this is cut peripherally, the nodule will naturally seem to have no connection with the membrane of Bruch. Again, while it is true that the pigment epithelium in many cases shows alterations, these have no constant relation in distribution to the colloid bodies, as has been shown by Kerschbaumer, and are to be regarded like the colloid bodies themselves as pathological, or in some cases as senile changes. The proof of cause and effect, therefore, is inadequate, and definite transitional forms have not been sufficiently clearly described and figured. Another very serious difficulty consists in the fact that the bodies, even when of large size, remain covered with epithelium, often flattened and depig-

mented, but seldom broken through (Pl. XVI, Fig. 1). Why should this be so if they arise from one or several pigment cells? Would the swelling cell not rather push its neighbours aside and remain uncovered? The explanation has been put forward that adjacent cells grow over, but why should they do so, and if they did, why should they form in so many instances a single uniform layer? It is surely more likely that the excrescences have a uniform covering, because they originated underneath the epithelium and merely raised it up. Over small nodules the epithelium will often be found to all appearance quite unaltered. Another explanation, still more unlikely, is that only part of the cell becomes involved in the degeneration, while the nucleus and unaffected part of the protoplasm form the well-stained lining. But this is surely supposing a thing very unlikely in the life history of an individual cell, nor are the cells firmly adherent to the excrescences as they ought to be if the latter were formed from part of their protoplasm.

Again, the size to which single nodules may grow (Pl. XVI, Fig. 1) is against their origin from one cell and strongly in favour of an origin by deposition or secretion; no case of a cell expanding to so great a size can, I believe, be produced in pathology. The remark does not, of course, apply to tuberculated or compound nodules such as are often found, since these might arise from the fusion of many cells. Nor does this exhaust the indictment against direct transformation; in the earliest stages the excrescences never separate with the pigment epithelium, but always remain firmly attached to the membrane of Bruch, although it is said that when large and standing upon a thin pedicle, they may break off and even be found in the outer layers of the retina. Again, Donders himself has shown that they react in all respects to reagents like the membrane itself, being highly resistant to water, alcohol, ether, acids, alkalies, mechanical injuries, etc., and failing, like the membrane itself, to take on the stain for amyloid substance.

A chain of arguments is thus raised against an origin

by direct transformation, each link of which seems to furnish proof for the second theory—that the excrescences are formed by deposit from the cells of the pigment epithelium in the same manner as in all probability the membrane itself was formed. The case in favour of this hypothesis, which was first stated by Heinrich Müller, may be put thus: In an early stage the bodies appear histologically to be simple localised bulgings inward of the membrane; they show no constant relation in localisation to those changes in the pigment epithelium, found in old and diseased eyes, which have been described as intermediate in the process of transformation; single nodules may grow to a large size while still remaining covered with a well-marked unicellular layer of epithelium; they do not separate with the epithelium when the latter strips off; they react to chemical, mechanical, and staining agents in all respects like the true membrane. In addition the analogy of the outgrowths of the membrane of Descemet may be cited. These also show no appearance of arising by transformation of the endothelial cells, but present themselves as localised inward bulgings of the membrane itself, lined by a well-preserved single-layered endothelium. In the case of the membrane of Descemet also, the proof is very complete that the endothelial cells are capable of laying down homogeneous substance, witness the membranes which sometimes form on the front of the iris in cases of anterior synechiæ (see Wagenmann, etc.).* The case of the capsule of the lens furnishes, perhaps, an even more complete analogy, since, like the membrane of Bruch, it is lined by epithelial cells of epiblastic origin, and Mr. Collins has shown that these cells also are capable of laying down new homogeneous substance.†

How then are we to explain the statement so often and

* Wagenmann, Arch. f. Ophth., 1892, vol. xxxviii, pt. 2, p. 91; Müller, Arch. f. Ophth., 1856, vol. ii, pt. 2, p. 48.

† Collins, Trans. Ophth. Soc., 1892, p. 89 (fig. at p. 100). See also Leber, Sitzungsb. d. Ophth. Gesellsch. z. Heidelb., 1878, p. 33.

so definitely made by supporters of the transformation theory that the membrane of Bruch can be seen to run past colloid bodies and to take no part in their formation? If it can really be shown to be so, then in spite of the arguments adduced above to show that they *ought* to arise from that membrane, we must either admit ignorance or find some new mode of origin for them. Nor can the statement be dismissed as founded upon a mere error of observation. There *is* such an appearance, as may be very clearly seen in Fig. 4, Pl. XV, and Fig. 1, Pl. XVI. Allusion has already been made to the fact that this would be produced if the nodule had a slender pedicle and a large expanded head, and if the periphery of this head were cut by the section, but not the pedicle. This, no doubt, is the explanation in some cases, but not in all, for it is a matter of experience that small excrescences, at least, are sessile, yet even in these the membrane of Bruch seems to go past unaltered (Pl. XV, Fig. 4). There is, however, another and most important factor in the structure of the membrane itself, a factor which seems to furnish the solution of the problem. In sections of ordinary thickness, prepared and stained in the usual manner, this membrane appears homogeneous or slightly granular (Pl. XV, Fig. 1). Yet even in early descriptions (Sattler, etc.), a finely reticular appearance of the outer aspect, and a tendency to split into two layers on macerating with strong salt solution were noted. Recently the key to this appearance has been given by methods of special staining. The reticular appearance is, in fact, due to a layer of very fine elastic fibres. In specimens stained with Weigert's elastic tissue stain, this is very plainly brought out (Pl. XV, Fig. 2). The separation into two layers is most distinct in the neighbourhood of the papilla where the membrane of Bruch is thickest, and the distinction is further emphasised here by the fact that the two portions end differently. The inner homogeneous portion, next the pigment epithelium, ends with the ending of the pigment epithelium, a further proof that it is a product of these cells. The outer elastic portion, which

can easily be seen with high magnification to be composed of a feltwork of exceedingly fine sharply stained elastic fibres, goes on into the substance of the papilla for some little distance, and finally terminates with a curious curly upturned end (Pl. XV, Fig. 2). It may be remarked in passing that Weigert's elastic tissue stain is specific only for elastic fibres and the elastica interna of vessels. A certain diffuse blue staining of a membrane, usually regarded as "elastic," is no proof that it contains the same substance as the true elastic fibres and membrane of Henle. For instance, the membrane of Descemet, the zonula, the lens capsule, the dilatator iridis, the sphincter pupillæ, and the homogeneous portion of the membrane of Bruch, all stain diffusely, but do not take on the intense blue staining which is characteristic of true elastic tissue.*

A further proof of the composite nature of the membrane of Bruch is furnished by its method of terminating towards the ciliary body. About the level where the pars plana gives place to the pars ciliaris retinæ the outer elastic layer becomes looser in texture, and being joined by elastic fibres from the general choroidal stroma, forms a meshwork of fine fibres. Through the openings of this meshwork connective tissue with a few fine vessels becomes insinuated, so that it no longer lies immediately underneath the pigment epithelium but is separated from it by a little distance. Tracing the fibres forwards they do not enter into the ciliary processes, but run straight on past their bases in the fine connective tissue between the ciliary muscle and the ciliary processes. Finally they end near the root of the iris not far from the elastic fibres given

* There is, however, some reason to suppose that the membrane of Descemet contains true elastic substance. It stains more deeply than the other membranes mentioned here, and fine elastic fibres may be seen passing off into the scleral tissues from its termination. There is, moreover, some evidence that the membrane of Descemet, like the membrane of Bruch, is composite in structure. It also has a tendency to split longitudinally, and in the case of colloid excrescences from it, an anterior layer may sometimes be seen to pass on unaltered, while a posterior layer bulges out to form the excrescence (see a picture in Wagenmann's paper, mentioned on p. 168).

off from the ligamentum pectinatum, but without coming into direct contact with these. The inner homogeneous part of the membrane, on the other hand, is described as entering into and following the sinuosities of the ciliary processes, forming in fact, a basement membrane for the pigment epithelium. Even in the anterior part of the true choroid, however, the homogeneous membrane is very thin, and in the ciliary processes it becomes difficult even in depigmented specimens to be sure that any definite membrane occurs. Rather the epithelium seems to rest directly on wavy connective tissue bundles, with at most the intervention of a linear basement membrane. There is at least in the ciliary processes no membrane staining specifically with Weigert's elastic tissue stain, and, indeed, except for an occasional isolated fibre usually accompanying a vessel, no elastic tissue in them at all.

The above details have been given in order to show that the membrane of Bruch which seems homogeneous when stained with eosin (Pl. XV, Fig. 1), can be resolved into two layers by special staining (Pl. XV, Fig. 2). It seems highly probable that the difference represents a difference in origin. The fine elastic fibres of the outer layer are in all respects similar to the elastic fibres found in the neighbouring choroid, and must, therefore, be looked upon as contributed by the choroid, since it is impossible to believe that definite elastic *fibres* could be laid down by the epiblastic pigment epithelium. The inner homogeneous layer on the other hand has all the appearance of a cuticular product laid down by the epithelium in the same manner as the lens capsule is laid down by its epithelium. The probability is, therefore, strong that it has been contributed by the pigment epithelium. It may be said that only the inner homogeneous layer ought to be reckoned as the membrane of Bruch (or lamina *vitrea*), and no doubt this would be convenient, but the present point is that the "membrane of Bruch" as seen in sections stained in the usual way includes both layers.*

* Or, on the other hand, it might be argued that the name should be used for the outer elastic layer, which would allow us to retain the synonym

Applying now these observations to the elucidation of the origin of colloid bodies, it will be found that there is much evidence in favour of the view that they arise from the inner homogeneous layer and from it alone. The argument would run somewhat as follows. The homogeneous portion of the membrane of Bruch is a cuticular product from the pigment epithelium, and in a similar manner under the influence of certain pathological stimuli, these cells may lay down irregular nodules of the same substance. On the other hand, the elastic portion is a mesoblastic product belonging in reality to the connective tissue of the choroid, and takes, therefore, no part in the formation of this secretion, but passes the nodules unthickened and unaltered. Since, however, it is homogeneously stained with eosin, an appearance is presented as if the membrane of Bruch went past unchanged and without having any connection with the colloid mass (Plate XV, Fig. 4). Hence has arisen the view that these excrescences are in origin wholly independent of the membrane of Bruch. Staining with Weigert's elastic tissue stain, however, will be found to solve the problem, for the unaltered membrane will be found to be only the outer elastic layer of the membrane of Bruch, while the colloid body is a true bulging of the inner homogeneous portion, and like it does not stain specifically with Weigert.

The formation of colloid bodies, however, is not the only instance of a pathological process which affects the two layers in a different manner. In general the elastic layer is more resistant than the other to noxious influences, and in some cases of chorio-retinitis it will be found that in the situation of an inflammatory patch the homogeneous portion is eroded while the elastic layer still holds, or that when both have

"lamina *elastica*" for "membrane of Bruch." The point is merely one of nomenclature and not of great importance so long as the details of structure are kept clearly in view. Perhaps the most convenient way would be to follow Smirnow in calling the homogeneous portion the membrane of Bruch and the elastic portion the "supracapillary" layer of the choroid, reckoning it thus as the innermost stratum of the choroid, as no doubt it is developmentally.

ruptured the elastic layer can be traced for a considerably longer distance than the other. An excellent instance of the different reaction of the two layers to pathological influences will be found in a paper by Mr. Nettleship in the last volume of the Transactions of the Ophthalmological Society.* The case was one of sarcoma of the choroid, and on its summit, between it and the retina, there was a layer of "dense wavy fibrous tissue" passing peripherally into "a thin structureless membrane bearing the pigment epithelium on its inner (retinal) surface. This epithelium-bearing membrane seems at first sight to represent the elastic lamina of the choroid, but the latter structure is in reality separate from it, being traceable, with interruptions, from one side of the tumour to the other, as a very undulating, highly refracting line which lies for the most part in the substance of the sarcoma close to its inner surface; towards the margin of the tumour the elastic lamina and the membrane bearing the epithelium meet, coalesce, and pass on together to the choroid." A figure (Fig. 29) is given, showing very clearly the homogeneous or faintly laminated inner layer and the wavy strongly marked outer layer. Through the kindness of Mr. Nettleship I have had the opportunity of examining sections of these structures, and there can, I think, be no doubt that the "epithelium-bearing membrane" above described is nothing else than the homogeneous portion of the membrane of Bruch, indeed a large number of colloid bodies spring from it. The "very undulating highly refracting line," on the other hand is the outer elastic layer, and stains characteristically with Weigert's stain. The case, therefore, furnishes the strongest possible proof of the composite nature of the membrane of Bruch and of the origin of colloid excrescences from the inner layer of it.

The conclusion reached is therefore in favour of the deposition theory as opposed to the transformation. Both theories have, however, this in common, that they presuppose an abnormal metabolism in the pigment epithelium. What

* Trans. Ophth. Soc., 1904, vol. xxiv, p. 93; fig. on p. 100.

the stimulus or lack of stimulus may be, which results in this altered metabolism, one cannot presume to say. It is in part, no doubt, definitely pathological, since they occur very constantly in eyes, the subject of extensive destructive changes, but in part also it is to be regarded as almost a normal change, since they occur in a large proportion of senile eyes. Without wishing to draw any close analogy, a comparison may be instituted between these changes and the changes which occur in endarteritis. In the latter case also the lesion may be a definite response to a pathological stimulus (in the neighbourhood of gummata for instance), or may, on the other hand, almost be regarded as a normal senile change.

It may be of interest to append a short historical *résumé* of the growth of our knowledge of the minute anatomy of colloid bodies—touching only upon the chief works, for the literature of the subject is very great, and much of it does not require revival. The general conditions under which they occur need not be discussed, since this paper has not dealt with this aspect of the subject. They have been found in very numerous diseases of the eye, but probably stand in essential relation to none of them.

It is a curious fact that the much rarer outgrowths of the membrane of Descemet were described before those of the membrane of Bruch—by Hassall, in 1849. Colloid excrescences were demonstrated in a single instance by Wedl, in 1854, but the first full description is by Donders, in 1855. Donders believed that it was the cell-nucleus which became the colloid body, and is the founder of the school which derives them by direct transformation from the pigment epithelium. In the same year Heinrich Müller had demonstrated them at a Würzburg medical society, and in the following year (1856) he published his views *in extenso* in a work full of careful observation and description, and still well worth a perusal. This was the foundation of the deposition theory, so that both schools were practically founded

in the same year. The intercalation of RUDNEW'S work (1871) may be disregarded, but in 1874, Donders's original hypothesis was modified by DE VICENTIIS, who pointed out that the protoplasm was a more likely seat for the deposit of abnormal products than the nucleus, and this is the view with modifications of detail which has obtained among supporters of the transformation theory to the present time. The original form of the theory was speedily abandoned, and in 1876 DE WECKER states that the opinion "that these vitreous knobs arise by colloid degeneration of the nucleus of the epithelial cell seems to be entirely given up." Adhesion is given to this modified theory by DA GAMA PINTO (1882), DIMMER (1885), and DE BONO (1891). The best of these works is Dimmer's—the others need not be consulted.

Turning now to the development of Müller's theory, we find LEBER in several places steadily supporting it. MEYER also gives it his adhesion (1877). Ossification is first described by ALT in the same year, but the presence of connective tissue in the centre of the excrescence, a rare appearance, but one undoubtedly related to the occurrence of true ossification is only mentioned in 1895 by LEBER. Ossification is also shown in a plate in PAGENSTECHER and GENTH'S Atlas, but its exact position is doubtful.

In 1892 appeared an important work by KERSCHBAUMER, giving a description of the earliest appearance of the excrescences as homogeneous or finely granular thickenings of the membrane. It is here pointed out that there is no necessary correspondence in distribution between the colloid bodies and the changes in the pigment epithelium. The author, therefore, does not favour the transformation theory, and though it is not expressly so stated, may probably be reckoned an adherent of MÜLLER'S.

Coming now to more recent works, we find most of them supporting the transformation theory. In 1902 we have HOFMANN'S paper, with a new theory of origin as mentioned in the text. RUMSCHEWITSCH (1904) seems to believe that the excrescences commence as a deposit from the cells, but

that later the cell substance itself becomes transformed into colloid material. PES in the same year denies all connection with the membrane of Bruch, and gives their origin either as from transformation of epithelial cells, or from sclerosis of surface papillæ which he describes as the result of inflammation in the middle and outer layers of the choroid. Finally, SCHIECK (1904) is a supporter of the transformation theory.

Cases which have both been seen clinically and examined pathologically are rare in the literature. LIEBREICH described the first in 1858, and the only other which I have been able to find is one by NAGEL in 1875—the year in which HUTCHINSON and TAY described the condition since known in England as "Tay's choroiditis," which they correctly presumed to be due to these excrescences. I have in one case been able to observe them clinically in one eye, and to find them microscopically in the other eye of the same patient, and possibly this is not an uncommon experience.

It is impossible here to go fully into the literature of the normal structure of the membrane of Bruch, but the following papers may be merely mentioned. Most of the older accounts are founded on SATTLER'S (1876) description. Of recent investigations, especially with Weigert's stain, SMIRNOW'S (1899), should be consulted for the general structure. A very excellent description of its ending towards the ciliary body will be found in SALZMANN'S (1900) work on the zonula. Figures of its ending towards the papilla are given in a paper by SAGAGUCHI (1902), but his explanation differs from that given in the text. I omit all mention of the clinical aspect of the subject.

FIG. 1.

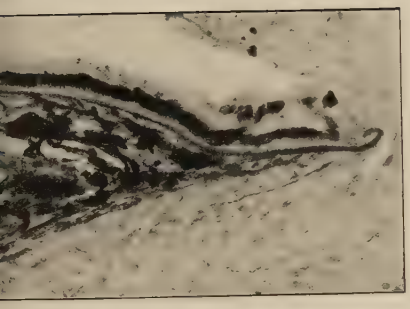

FIG. 2.

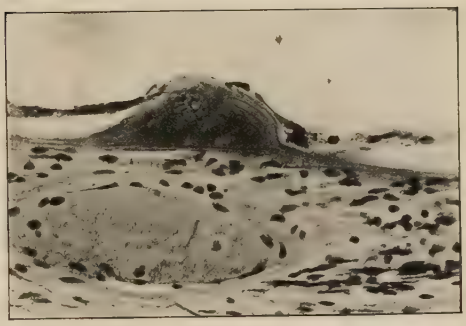

FIG. 3.

FIG. 4.

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FIG. 1.

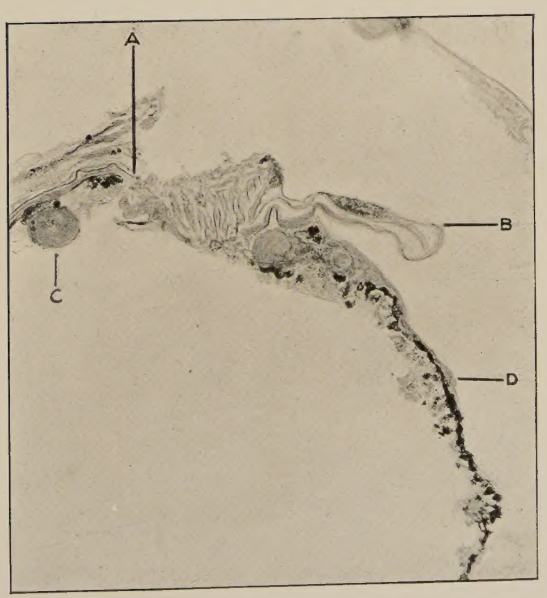

FIG. 2.

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Description of Plates XV–XVI.

[I am indebted to Professor Wintersteiner, of Vienna, for permission to use the specimens from which Fig. 3, Pl. XV, and Fig. 1, Pl. XVI, were taken, and to Mr. Nettleship for the specimen photographed in Fig. 2, Pl. XVI.]

Plate XV, Fig. 1 (× 200).—Membrane of Bruch in the neighbourhood of the papilla stained with hæmatoxylin and eosin. It has a somewhat granular, but uniform appearance, and there is no division into layers.

Fig. 2 (× 200).—The membrane of Bruch at the papilla stained with Weigert's elastic tissue stain. It consists of an inner homogeneous or somewhat granular layer, and a thin deeply stained outer line. In the actual specimen this outer layer was coloured dark blue—the specific stain for elastic tissue. The two portions end differently, the inner at the same place as the pigment epithelium, while the outer projects for some distance into the substance of the papilla, and terminates in an upturned end.

Fig. 3 (× 200).—A colloid body stained with hæmatoxylin and eosin. It appears as a simple sessile bulging of the membrane of Bruch. It is covered by a single layer of flattened epithelium. In its centre there is a small clearer area, probably commencing degeneration (specimen by Professor Wintersteiner).

Fig. 4 (× 200).—A small colloid excrescence stained with Weigert's fluid. A strongly marked line runs past it, which is stained deep blue in the specimen and might be taken for the whole membrane of Bruch, of which however, it is only the outer part (*cf.* Fig. 2). The colloid body seems to have no connection with it.

Plate XVI, Fig. 1 (× 200).—Two large laminated colloid bodies stained with hæmatoxylin and eosin. Beneath them and apparently quite unconnected with them, there is a fine highly refracting zig-zag line. This is the outer elastic layer of the membrane of Bruch thrown into folds by the cicatricial shrinking which has taken place in the choroid (case of phthisis bulbi). Although the bodies are so large they are still covered by an unbroken but flattened and partially depigmented layer of epithelium (specimen by Professor Wintersteiner).

Fig. 2 (× 90).—(From a case of Mr. Nettleship's, reported in Trans. Ophth. Soc., vol. xxiv, p. 93.) To show the behaviour of the membrane of Bruch over a choroidal sarcoma. The two layers are well seen above, and from the inner homogeneous, a colloid body (C) springs. Their relations are here normal. At (A) the outer elastic layer breaks off suddenly. It reappears again as a zig-zag line ("very undulating, highly refracting line" of Mr. Nettleship's description), but ends finally at (B). The inner homogeneous layer (D), on the other hand, continues across the figure ("epithelium and 'colloid'-bearing layer"). Several colloid bodies are seen in it—the letter points to two small ones—and there were a number of others beyond the borders of this field and far away from the ending of the elastic layer.

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